fibers following as a secondary phenomenon This condition he proposed to separate from other forms of myelitic spinal disease on the ground that it is a disease *sui generis* Five years later an article appeared by the English observers, Russell, Batten, and Collier, containing a description of the same class of cases, together with evidence pointing to associations with a toxin that causes more or less injury to the blood-making organs In the United States, besides the important early articles of J J Putnam and C L Dana, excellent papers on the subject have been published by Taylor and Waterman, by Barr and McCarthy, by Billings, by Grinker, and by Camac amd Milne The opinion that there is no essential distinction between so-called "pernicious anemia accompanied by changes in the spinal cord" and "combined sclerosis of the cord accompanied by anemia" has been steadily gaining ground, and is now generally accepted The difference between the two groups of cases lies in the fact that in some persons the anemic changes make their appearance earlier and are more severe than those in the spinal cord, whereas in other persons these conditions are reversed The patient before us this morning is an interesting example of the second type, namely, that in which the symptoms indicate that the cord changes are definitely established, though the blood changes have only begun to appear

The patient, C E C , is a married man, forty-five years old He was admitted to the hospital less than a week ago, complaining of inability to walk and of a sense of constriction at the waist, as though a bandage were tied around it His family history contains nothing bearing upon his present illness and his past history is unimportant except for the fact that he had a Neisserian infection about twenty years ago When you hear of inability to walk, accompanied by a binding sensation around the waist, what system would seem to you to be involved?

STUDENT The nervous system

DR BARKER Yes Now in studying conditions associated with the nervous system we follow certain rules In the diagnosis of such affections, we pass through three stages First of all, we accumulate the data, second, we try to make a topo-

graphic diagnosis, if possible, of the changes taking place in the nervous system, that is, we determine the locality of the lesion or lesions, third, having localized the lesions, we proceed to ascertain their nature. We shall begin here, therefore, by collecting the necessary data.

The patient's present illness began about a year ago, when he noticed a slight numbness in the fingers of both hands, most marked in the middle fingers. (To patient) Were you quite well up to that time?

PATIENT Yes

DR BARKER About two weeks later he noticed a similar sensation in his toes, the numbness being succeeded by a feeling of coldness. This numbness in the toes gradually extended up the legs, until, in about three months, it reached the waist, at this time the patient began to experience also the sense of constriction already mentioned There was no extension of the numbness in the upper extremities, progress in the numbness was entirely confined to the lower part of the body As the numbness increased the patient began to feel weak in the legs, soon after which he began to limp on the right side About three months ago he recognized that he could not control the escape of gas from the rectum Has there been any incontinence of urine?

STUDENT No, but he says he sometimes has trouble in starting the flow

DR BARKER The weakness in the lower extremities has grown gradually worse, until now he is practically unable to walk at all Some time ago he noticed that when he stood up with his eyes closed he was in danger of falling Since the onset of his illness he has been depressed, and he states that he is emotionally upset more easily than formerly In other respects the symptoms have remained unchanged (To patient) How long is it since you were obliged to give up walking?

PATIENT About five weeks

DR BARKER These are all the positive data in the anamnesis bearing upon the diagnosis. (To patient) Have you had headaches?

PATIENT No

DR BARKER Any dizziness?

PATIENT Only since I have been in the hospital

DR BARKER Any ringing in your ears?

PATIENT No

DR BARKER Any cough?

PATIENT No

DR BARKER Any shortness of breath?

PATIENT No

DR BARKER Any palpitation of the heart? Does your heart ever beat fast?

PATIENT No

DR BARKER Have you a good appetite?

PATIENT Yes

DR BARKER Is there ever any gas coming from the stomach?

PATIENT Sometimes

DR BARKER Do you ever have any nausea or vomiting?

PATIENT Occasionally

DR BARKER Are your bowels regular? Have you any constipation or diarrhea?

PATIENT I was constipated sometimes when I was up and about, and it has been worse since I have been in bed

DR BARKER Have you any trouble from hemorrhoids or piles?

PATIENT A little, sometimes

DR BARKER Is there ever any bleeding?

PATIENT No

DR BARKER No bleeding hemorrhoids (To student) Have you anything of importance to report about the patient's habits?

STUDENT He has never been employed in manual labor For the last three years he has been a watchman and before that he was in a mercantile business

DR BARKER How about potatorium? (To patient) Do you ever drink anything?

PATIENT For fifteen or twenty years I used to drink three or four glasses of beer a day, but I have given it up now I have never drunk whisky and I have never smoked

DR BARKER   Has he had any infections?

STUDENT   About twelve years ago he was in bed for a week with what was called "typhomalaria."

DR BARKER   It may have been malaria. It could hardly have been typhoid unless it were a very mild attack. Has he ever been operated upon?

STUDENT   No

DR BARKER   Is there any history of trauma?

STUDENT   No

DR. BARKER   So much for the anamnesis   Examination on admission to the dispensary was negative except on the neurologic side   How about his teeth? There is some pyorrhea. Are there any dead teeth?

PATIENT   I have had several teeth extracted   I think they were dead

DR. BARKER   Open your mouth, please. Yes, there are still several teeth with large fillings present and others that look discolored   Probably there are still some dead teeth here, but no x rays have been taken as yet, as he has been here only a few days and has not yet been down to the dental clinic   Examination of the head was negative, was it not?

STUDENT   Yes.

DR. BARKER   There is no struma, the neck is negative The heart and lungs are negative. Abdominal palpation was not wholly satisfactory, because the abdomen was held so rigidly

Let us begin our objective study of his nervous functions by examination of the motility   Here we find considerable weakness, especially in the legs, and some spasticity   (To patient) Bend your right leg, please   Is that all you can do? Now use your full strength and try to prevent me from bending your knee. He has but little power in the muscles of this leg Let us try the left leg in the same way   You see there is about the same condition of things as in the right leg   Both the flexors and extensors are evidently weak   (To patient)   Now shove down as hard as you can   Do it again, please. Now the other foot   You can see the evidence of weakness plainly

on both sides, but it is greater on the left side (To patient) Now I want you to make a circle in the air with your right foot It is a question, at first, whether the tremulous, indefinite movements he makes are due to weakness or to ataxia (To patient) That's better Now try to do it with the left foot. As hard as you can I am trying to prevent you and I want you to resist me All the muscles of the lower extremities are obviously weak

Now let us test the muscles in the upper extremities (To patient) Grip my hand with your own right hand, please As hard as you can Now with your left hand His grip is very poor on both sides (To patient) Pull my hand as hard as you can Now shove it. Now do the same thing with your left arm The flexors and extensors of the elbow seem to be fairly strong

Next we will test the abdominal muscles First of all, we will ascertain the presence or absence of Beevor's sign According to Beevor, if there is any paralysis of the lower segment of the recti muscles, there is a riding up of the umbilicus when the patient tries to raise his head and sit upright (To patient) Sit up, please No, try again without using your arms Fold them across your chest There is certainly no outspoken paralysis of the abdominal muscles and Beevor's sign is not present The abdominal muscles may be a little weak, but we must bear in mind that he has not used them for some time

Now let us test the muscles of the head and neck (To patient) Wrinkle your forehead Frown Show your teeth, please The muscles innervated by the seventh nerve contract well Close your jaws tightly together as though biting hard His masseters contract strongly What nerve did I test then?

STUDENT The motor branch of the fifth nerve

DR BARKER Yes The masseter muscles are supplied by the mandibular branch of the fifth (To patient) Look at my finger, please Look at it as I move it from side to side Look up Look down The eye muscles work well There is a slight von Graefe's sign and a slight Dalrymple sign, but neither of these is well marked There seems to be nothing

wrong then with the third, fourth, and sixth cerebral nerves
We have tested the motor part of the fifth and the seventh
(To patient)   Can you swallow without difficulty?

PATIENT   Oh, yes.

DR BARKER   The ninth and tenth nerves seem to be work
ing satisfactorily

Can you tell me the name of the eleventh cerebral nerve?

STUDENT   The *nervus accessorius*

DR. BARKER   Yes   How would you proceed to test it?

STUDENT   I am afraid I don't know

DR. BARKER   What muscles does it supply?

STUDENT   The sternocleidomastoid muscle and the upper
part of the trapezius

DR. BARKER   Yes   Then we can determine its condition
most easily by testing the activity of the sternocleidomastoid
(To patient)   Turn your head to the left, please.   Now to
the right.   You see, there is no paralysis   Now let us test the
twelfth nerve, that is, the hypoglossal or motor nerve of the
tongue.   (To patient)   Put out your tongue, please   You see
there is no difficulty there—no paralysis of the hypoglossus

That concludes our examination of the motor activities of
the cerebral nerves   Has the patient's sensation been tested?
We shall leave the reflexes until a little later   What was found
as regards sensation on examination in the ward?

STUDENT   Rough tests of sensation showed impairment of
the tactile sense on the medial surfaces of the lower extremities
just below the knee and also on the dorsum of the foot.

DR. BARKER   You found a little loss of tactile sensitivity
then?

STUDENT   Not very much.

the tempo of the stimulation intervals   Certainly, at present, he recognizes every stimulus promptly as far as touch is concerned   The only evidence of impaired sensation that he has shown in the ward is a slight dulling of perception on the inner surface of the thighs   Now let us test for sensations of heat and cold   (To patient)   Close your eyes, please, and tell me whether you feel something warm or cold   As you see, I am testing very roughly   He recognizes warmth correctly every time   His recognition of cold is not quite so acute, but it is possible that the perception of cold may be confused with that of touch because the breath stirs the hairs on the surface of the extremities and so stimulates the sense of touch Did you notice any disturbance of temperature-sense in the ward?

STUDENT   No

DR BARKER   How about pain?

STUDENT   No analgesia was made out

DR BARKER   Let us try for ourselves with a pin   (To patient)   Tell me when you feel the point of the pin, but when you feel the head of the pin do not say anything

PATIENT   Now   Now   Now

DR BARKER   You see he recognizes the prick of a pin everywhere   Now let us find out if there is any bathyanesthesia   Bathyanesthesia is a term covering the loss of deep sensibility   When this is lost or diminished we have to do not only with a loss of sensibility as such, but with a loss of the unconscious centripetal impulses that play an important part in the maintenance of muscular tonus and the co-ordination of muscular activity   (To patient)   Close your eyes, please Now tell me whether I am moving your great toe upward or downward?

PATIENT   I can feel you touch it, but I don't feel it move at all

DR BARKER   You can all of you see me move his toe passively   I would have you note that a patient whose nervous system is normal can distinguish the direction of any movement that you can see   (To patient)   Let us try the other foot

PATIENT   I can feel you touch it, but I can't tell whether you are moving it up or down.

DR. BARKER   There is plainly disturbance of position-sense and of the sense of passive movement in both great toes, indicating definite bathyanesthesia. Now let us apply the same test a little higher up   (To patient)   As I bend your ankle, tell me whether I am moving the foot up or down?

PATIENT   I can't tell

DR. BARKER   You could all, even those of you at a distance see that I cause a considerable excursion of the foot, but the patient was not conscious of it.   Now for the knee   In making this particular test you must take care that the leg is placed half way between flexion and extension.   (To patient)   Close your eyes and tell me whether I bend your knee or straighten it.

PATIENT   I can't tell which

DR. BARKER   Did I move it at all?

PATIENT   I can't say

DR. BARKER   Now we will try the other knee   (To patient)   Can you feel any movement now?

PATIENT   No, none at all

DR. BARKER   This is a really striking example of bathyanesthesia.   Though his knee is bent and straightened, he does not feel the changes   Now let us test the upper extremities   (To patient)   Close your eyes, please, and tell me whether I am moving your hand up or down

PATIENT   Now you are moving it upward.   Now downward   Upward   Downward.

DR. BARKER   Here he recognizes passive movement and its direction promptly

Next, we shall test the wrist.   Then the elbow   You see that in each case, even with such a slight amount of excursion as I am making now, he recognizes the nature of the movement correctly   The bathyanesthesia seems, then, to be confined to the lower extremities

Has there been any disturbance of the pupillary reflexes?

STUDENT   No

DR. BARKER   No optic atrophy or colour loss?

STUDENT   No   The disks are clearly outlined and there is
no sign of atrophy

DR BARKER   How about his hearing?

STUDENT   Fifteen years ago he had an attack of earache in
his right ear, and ever since then he has been slightly deaf on
that side, but not much so

DR BARKER   Is his sense of smell all right?

STUDENT   Yes

DR BARKER   Taste also?

STUDENT   So far as we have yet observed

DR BARKER   The special senses will have to be tested more
closely later on, but they seem to be quite normal as far as can
be determined by a rough examination

Now, we know that in this patient there is marked bathyan-
esthesia of the lower extremities, and if there is bathyanesthesia
there should be something else also   (To patient)   Close your
eyes once more, please   Now put your right heel on your left
knee   You see at once that he cannot make adequate measure-
ments   There is hypermetria, that is to say, he overmeasures
the distance to be covered   (To patient)   Keep your eyes
closed, please   Now I will put your right heel on your left
knee, and I want you to run your foot steadily, straight down
the shin   You see how his foot wanders in trying to accomplish
this movement   Dynamic ataxia is well marked in the lower
extremities   It is always present when there is bathyanesthesia,
but this is a wonderful example of it   (To patient)   Now raise
your right foot 6 inches from the bed and hold it steadily in
that position   This is the test for static ataxia

PATIENT   I can't tell how far off my foot is from the
bed

DR BARKER   You see that he cannot form any correct
conception of distances   (To patient)   Now I am going to
raise your heel a foot from the bed and I want you to hold it
steadily there   Is that a foot from the bed?

PATIENT   I can't tell

DR BARKER   You see he holds the foot with a fair degree
of steadiness, though he has no conception of the distance from

the bed at which he is holding it. There is very little static ataxia, though the dynamic ataxia is well marked

Now let us investigate the question of ataxia in the upper extremities There was no bathyanesthesia of the arms, we shall probably find that there is little or no ataxia (To patient) Close your eyes and touch your nose with the tip of your left forefinger, please Now try the same thing with the other hand You see he accomplishes this maneuver with fair success There is only a slight miscalculation

The whole state of things here is very interesting There is good postural sense and passive motion in the arms, with very little ataxia. In the lower extremities conditions are exactly the reverse.

Now let us test for hypertonicity or hypotonicity of the muscles (To patient) Let this leg go just as loose as possible, please. You see the minute I start to move that leg it goes into a condition of hypertonicity that interferes with passive motion. I would have you notice that we have here an unusual condition, in which there is loss of deep sensation, associated with hypertonicity This is the opposite of what we should expect. In general, bathyanesthesia is associated with hypotonicity You will recall the conditions in tabes dorsalis In the upper extremities there is no bathyanesthesia and there is no hypertonicity

Now we may proceed to test the reflexes What did you find out about them in the ward?

STUDENT There was a little hyperactivity of the deep reflexes

DR. BARKER Only a little? At this moment there is more than a little. At present there is, as you can see, an extreme degree of hyperactivity of the knee-jerks You see an exquisite patellar clonus on both sides The ankle-jerks also are hyperactive, it is rather difficult to test the ankle-jerks when the patient is lying in bed Still, we can perceive that in this case there is marked exaggeration of the Achilles jerk You will observe that the hypertonicity in the lower extremities is corroborated by the exaggerated reflexes, whereas in the upper

extremities, where there is no hypertonicity, the radial, the biceps, and the triceps reflexes are all about normal   Let us turn to the superficial reflexes   You see that the abdominal reflexes are present   In what disease are the abdominal reflexes usually absent on both sides?

STUDENT   In multiple sclerosis

DR BARKER   Yes   In this case, as you have seen, the abdominal reflexes are present, both above and below   When we try the plantar reflexes by tickling the soles of the feet we find that there is a positive Babinski in both feet, but it is accompanied by a marked tickle response   (To patient)   Does that hurt you?

PATIENT   Yes indeed, it does

DR BARKER   You perceive it causes very evident suffering Painful soles of the feet on stimulation is a neurologic phenomenon that is sometimes of diagnostic significance   In what condition do we find it   Can anyone answer?

STUDENT   In alcoholic polyneuritis

DR BARKER   Yes   Whenever you find the plantæ painful on testing for the plantar reflex you should always think of potatorium   The Gordon reflex is positive here   Oppenheim's sign is not easily elicited in this patient   There seem to be painful points along the peripheral nerves   This is important and the Valleix points should be carefully tested, because one of the features of alcoholic neuritis (pseudotabes) is the presence of such painful points   (To patient)   You said you had been in the habit of drinking beer?

PATIENT   For fifteen or twenty years I drank three or four glasses of beer a day, but for the last two years I have taken very little

DR BARKER   Three or four glasses a day for fifteen or twenty years, though a mere drop compared with the amounts imbibed by some beer-drinkers, means, in the aggregate, a good deal of alcohol   Still, for two years he has been abstemious Has the patient shown any hallucinations? Delusions? Depression? Disorientation?

STUDENT   No, nothing of the kind

Dr. Barker   There is very little, then, in the history or
in the results of the examination that points to disorder of the
cerebral functions

I think we have now collected the necessary data bearing
on the nervous system, and we have spent a good deal of time
in doing so   Now let us proceed to summarize our neurologic
findings   (The patient at this point was taken back to the
ward)

We have inability to walk with pronounced paresis and
ataxia of the lower extremities associated with hypertonicity of
the muscles   In the upper extremities there is a little paresis
without hypertonicity   The reflexes in the lower extremities are
hyperactive, so much so that there is actual clonus   There is
also marked bathyanesthesia of the lower extremities without
surface anesthesia   There is very slight sphincter disturbance
The tactile perception seems nearly normal   Apparently there
is no involvement of the cerebral nerves   The eyes seem normal
The pupils are equal   The Argyll Robertson pupil is not present
All the symptoms have come on rapidly, that is, within the last
year   They include certain important subjective symptoms,
namely, tingling sensations in the fingers and toes, extending
up the lower extremities to the waist, where there is a sense of
constriction   The important objective sensory finding is the
bathyanesthesia associated with the marked dynamic ataxia of
the lower extremities.

Let us endeavor now to localize the lesions   Dc
the condition functional or organic?

Student   I think it is organic.

STUDENT   The part below the brain

DR BARKER   Yes, for there is no disturbance of the functions of the cerebral nerves, nor of the functions of the cerebrum and cerebellum   The eye-grounds are negative, there is no temporal pallor of the optic disks and no Argyll Robertson pupil Everything seems to rule out the cerebrum

If the organic nervous condition with which we are here dealing is below the brain, are we to think of it as being in the spinal cord itself or in the peripheral nerves? Before actually deciding this point I shall ask you to consider, since the head is free, what parts of the body below the head are chiefly affected

STUDENT   The lower parts

DR BARKER   Yes   The symptoms are distinctly more marked below than above the level of the middle of the body But the numbness of the fingers and the weakness in the hands shows that there is some involvement above the middle of the body as well

The next point for us to consider is whether this condition is a spinal-cord or a peripheral affair   Let us take, first, the question of the disturbances of motility   Are they due to lesions of the upper or of the lower motor neurones? What do you think?

STUDENT   I should think the upper motor neurons

DR BARKER   Why?

STUDENT   From the fact that the reflexes are hyperactive, and besides there is a positive Babinski reflex on each side

DR BARKER   You are right   Such a spastic hyperactivity of the reflexes as we see here and the positive Babinski sign always point to lesions of the upper motor neurons   Now the upper motor neurons are situated entirely within the central nervous system   They do not enter the peripheral nerves   Let us recall the histology of the upper motor neurons   Where are the cell bodies belonging to the upper motor neurons situated?

STUDENT   In the motor area of the cerebral cortex

DR BARKER   Yes, chiefly in the anterior central gyrus and in the paracentral lobule   Describe, please, the course followed

by the axones that are given off by the cell bodies of these upper motor neurons

STUDENT They traverse the centrum semiovale, pass through the internal capsule and the foot of the cerebral peduncle, and enter the brain stem, having gone through the basilar part of the pons, they form the pyramids of the medulla, most of the fibers of the pyramids undergo decussation in the medulla oblongata, the crossed fibers passing down to form the lateral pyramidal tract of the spinal cord, the uncrossed fibers going to form the direct pyramidal tract of the anterior funiculi All these axones end in arborizations about the cell bodies and dendrites of the anterior horn cells in the gray matter of the spinal cord, thus synapsing with the lower motor neurons

Could the pyramidal tract be affected from the cortex?

STUDENT I think it could

DR. BARKER Yes, it could be. If the cell bodies were injured, the secondary degeneration would extend to the spinal cord But if the lesion were situated there, we should expect to have some evidence pointing to disturbed functions of the upper motor neurons that synapse with the lower motor neurons of the cerebral nerves Could the pyramidal tract be injured below the head—say, in the spinal cord itself? If so, would the lesion be in the anterior funiculi, the posterior funiculi, or in the lateral funiculi?

STUDENT In the anterior funiculi for the uncrossed pyramidal tracts and in the lateral funiculi for the crossed tracts

DR. BARKER Yes We have good evidence that the pyramidal tracts below the medulla oblongata have been injured in this patient, and the lateral funiculi are doubtless mainly involved It is possible that there is some involvement of the direct pyramidal tract in the anterior funiculi as well

Now let us turn to the localization of the lesions causing the sensory disorder The presence of bathyanesthesia without surface anesthesia in the lower extremities is of great diagnostic importance One must know a good deal about the anatomy and the physiology of the nervous system, and have clear ideas of the topography of the conduction paths of motor and sensory

impulses in order adequately to localize disturbances of nervous functions such as this patient presents   Professor Sabin has given you a good drill in the anatomic laboratory and Professor Howell has reinforced this in his lectures in the laboratory of physiology   Without such knowledge it would be impossible to work out clues like these   Bathyanesthesia, without surface anesthesia, points to an elective lesion in the sensory conduction path   Now the general sensory conduction path consists of three or four sets of superimposed sensory neurons   First, there is the peripheral sensory neuron, the cell body of which is situated in a spinal ganglion, the long axone-like dendrite, extending to the periphery of the body and the long central axone, entering the spinal cord through the posterior root of a spinal nerve Once within the cord, this axone gives off collaterals to the gray matter, and then, if it conducts impressions of muscle sense, extends for a longer or shorter distance upward in the posterior funiculus of the cord, first in the funiculus cuneatus of Burdach, and later, in case it is a very long fiber, in the funiculus gracilis of Goll, ultimately terminating in a synapse upon the cell body of a sensory neuron of the second order   The axone of the latter crosses in the sensory decussation of the medulla and passes onward in the medial lemniscus to end in the ventrolateral nuclei of the thalamus   There the path is continued by a sensory neuron of a still higher order to the cerebral cortex (posterior central gyrus)

Now, in the peripheral nerves, the fibers for pain, touch, and temperature sense are intimately mixed with those for deep sensibility (muscle sense, postural sense)   It is within the spinal cord that the conduction paths for the several modalities of sensation first pursue more or less isolated courses   The absence of lancinating pains in the lower extremities and of severe spontaneous pain in root zones, as well as the absence of segmental anesthesia and of anesthesia in areas that correspond to peripheral nerve distribution, are all evidence against involvement of either the peripheral nerves or of the posterior roots of the spinal nerves in their extramedullary course   But the presence of ataxia and of bathyanesthesia without surface anesthesia

point strongly to an intramedullary lesion, namely, of the intramedullary continuations of the axones of the peripheral sensory neurons within the posterior funiculi. On the other hand, the paths in the spinal cord for the upward continuation of pain and temperature impulses, namely, Gower's tracts, appear not to be involved, despite the evident lesions of the adjacent pyramidal tracts in the lateral funiculi. Taking all these points into consideration, I think we may be quite sure that we have, in this patient, to do with combined injury and degeneration of parts of the posterior and lateral funiculi of the cord. We have, therefore, fairly satisfactorily localized the lesions. The topographic diagnosis points to these posterior and lateral funiculi of the white matter on both sides, that is to say, we have to deal with combined changes in these four divisions of the white matter of the spinal cord. So much, then, for the localization of the lesions.

The next point to be considered, as far as the time at our command allows, is the nature of these lesions that we have localized. It really requires more than one hour to deal adequately with such an interesting case as this. In the few minutes that remain I shall try to draw some valid conclusions regarding pathogenesis.

First of all, we might be dealing here with taboparesis, that is to say, with a combination of locomotor ataxia with general paresis of the insane—a *parasyphilis*. We know that in 48 per cent. of autopsies on general paretics there are lesions in the posterior and lateral funiculi of the spinal cord. But in this case we can rule out taboparesis. How?

STUDENT By the absence of the Argyll Robertson pupil.

DR. BARKER Yes. This fact is strongly against tabes and against general paresis. Another fact against both these conditions is the fact that the cerebrospinal fluid has been tested in this patient and shows no increase in cells in 17 fields examined. Moreover, the Wassermann reaction in the spinal fluid is negative. The report on the blood Wassermann has not yet been handed in. It is true that the gold-sol test on the spinal fluid shows a luetic curve, but in the absence of any increase in the

cell count, and with negative globulin and Wassermann reactions, I think we can safely rule out both tabes and general paresis You might ask, Could it be an arrested tabes? I think not Some explanation other than syphilis must be found for the ataxic paraplegia of this patient

Next, we may consider the possibility of the existence of *multiple sclerosis* There are multiple lesions in the spinal cord and they are probably sclerotic lesions There are, however, three points that may be urged against a diagnosis of multiple sclerosis First, this patient is rather too old for it. Multiple sclerosis is essentially a disease of youth and makes its appearance usually between the fifteenth and the thirtieth year In the second place, the abdominal reflexes in this patient are little, if at all, affected, whereas in multiple sclerosis they are usually absent In the third place, symptoms or signs referable to the brain or to the optic nerves are always present in multiple sclerosis, whereas here there are no signs of cerebral involvement. So, for all these reasons and for others which might be adduced were there time, I think that multiple sclerosis may be ruled out

At this point we may ask ourselves whether we may not be dealing with a transverse myelitis with a partial involvement of the white matter of the cord—in other words, with a *myelitis transversa incompleta* We know that this disease can yield a clinical picture something like the one we have here The mode of onset and the mode of progress of the disease are wholly different in transverse myelitis from those recounted by our patient. No myelitic lesion at a single level could account for the phenomena before us So I think we may rule out *myelitis transversa*

These several exclusions bring us back to the diagnosis of the only condition that in my opinion accounts for the findings I may add that this opinion is shared by my colleague who is in charge of the neurologic department of the hospital, Dr H M Thomas, and also by those who have studied the patient in the wards of the hospital The condition is a form of *funicular myelitis*, sometimes called an *anemic focal intrafunicular leuko-*

One point of importance is the existence of oral sepsis in connection with many cases of funicular myelitis In this instance there is some oral sepsis There is also no free HCl in the stomach contents, indeed, there is a deficit of 20 acidity per cent In most cases of pernicious anemia with combined sclerosis there is a benign achylia gastrica

You have heard that the blood examination reveals the presence of 12 per cent of eosinophils This fact makes us think of the possibility of worm invasion We know that such invasion can produce a pernicious anemia Invasion of the intestine by the large fish-tapeworm, *dibothriocephalus latus,* is accompanied by a severe anemia Anemia due to this cause presents, clinically, all the symptoms and findings of a severe hemolytic anemia, but severe anemia in this country is rarely due to it. In Finland and among the Esquimaux *dibothriocephalus anemia* is not uncommon The explanation of the eosinophils in our patient has not yet been found, though doubtless further observation will provide it

Taking all the data into consideration, I think there can be no doubt that we are justified in making a diagnosis of funicular myelitis, or of combined sclerosis of the spinal cord, in which the anemic changes are slight and are late in making their appearance, though there must be outspoken changes in the spinal marrow

Colin Russel, in considering this group of cases, divides the course of the disease into three stages First, a period of mild ataxic paraplegia, occupying one-half to three-fourths of its whole duration Second, a period of complete spastic paraplegia, with loss of sensibility in the lower extremities and the lower part of the trunk, this occupies about one-half of the remaining time Third, a period of flaccid paraplegia covering the rest of the course in which there is elevation of temperature, general malaise, and asthenia, with an increase of the anemia In the present instance the patient seems to have entered upon the second stage As time goes on the anemia, asthenia, and general disturbance of metabolism will probably increase, though we shall do all in our power to arrest or to slow the process

I may mention here that only last week I saw another case of this kind in which the typical tingling of the fingers and toes, the oral sepsis, and the benign achylia gastrica were all present. The patient's red blood-cells, however, numbered 4,000,000, and his hemoglobin was 90 per cent. There was only a little poikilocytosis. I think there can be no doubt of the diagnosis, but it is interesting to have the case come under observation at such an early stage, especially as it will give us opportunity to try and see if it can be arrested at this point by energetic treatment.

Our time is exhausted, but before we close let us ask ourselves: What actually causes these lesions in the spinal cord? In answer, we are obliged to say that as yet we do not know. We do know, however, that the injury is in some way related to the blood-vessels that enter the white funiculi of the spinal cord. The first changes that have been observed at autopsy include a few sharply defined areas of sclerosis in the central part of the posterior funiculi in the cervical or lumbosacral regions, or else in the lateral funiculi in the middle cervical or in the thoracic cord. Proliferation of the neuroglia has also been observed with the formation of lacunæ. Somewhat similar changes can be seen in the lateral funiculi in the lumbar regions. The areas of degeneration are small at first, though they gradually enlarge; sometimes there is confluence of smaller foci into a larger area. Some poison evidently arrives through the blood-vessels and starts a degenerative focus, which spreads from its original site so as to make an ever larger focus. Secondary degenerations, of course, follow upon the focal destructive lesions. The involvement of the white matter of the cord is not confined to any specific kind of nerve fiber. Though it happens that the fibers of the sensory paths in the posterior funiculi and the fibers of the pyramidal tracts in the lateral funiculi are predominantly involved, we are dealing with a pseudosystemic process, not with a true system disease. The lesions transcend the system limits, it being more or less accidental that certain definite conduction paths fall within the destroyed areas. What the noxa is that injures the nervous

system on the one hand and the hemopoietic system on the other we must try hard to ascertain In investigating this problem it may turn out that the almost constant association with oral sepsis and with benign achylia gastrica is significant. You will note how unsatisfactory our knowledge of the real nature of the disease is as yet

To the student beginning· the study of clinical neurology the symptom-complexes presented by combined sclerosis of the posterior and lateral funiculi may seem particularly puzzling For in one case the symptoms pointing to the posterior funiculi may predominate, in another those pointing to the lateral funiculi may predominate, and in a third the symptoms may suggest almost equal involvement of the posterior and lateral funiculi Thus in a patient whose pyramidal tracts have suffered most, the hypertonicity, the hyperreflexia, and the paraparesis will be the striking symptoms, and a little ataxia, a little tingling and numbness in the fingers and toes, and slight bathyanesthesia may be almost the only symptoms pointing to the posterior funiculi The patient before us with his spasticataxic paraplegia, and inability to walk, is a good example of this type But in a patient whose posterior funiculi have suffered most, the clinical picture may much more closely resemble that of tabes dorsalis (ataxic gait, hypotony, loss of knee-jerks and ankle-jerks, bladder weakness), though a little paraparesis and positive Babinski signs may be present as marks of the injury to the lateral funiculi The only safe way to proceed, especially for the beginner, is the one I have indicated, that of first painstakingly accumulating the data regarding disturbances ' of motility, sensibility, and reflexes, second, carefully scrutinizing the data with reference to localizing marks, and, finally, through a consideration of the patient's history and status as a whole, arriving at a conclusion regarding the nature of the disease process and its pathogenesis

LITERATURE

Collier, J   Subacute Combined Degeneration, in Syst Med (Allbutt & Rolleston), 8th, London, 1910, vii, 786–804

Dana C. L. Subacute Combined Sclerosis of the Spinal Cord and its Rela
    tion to Anemia and Toxemia, Jour Nerv and Ment Dis New York,
    1899 xxvi 1–19
Henneberg R.   Myelitis und die myelitischen Strangerkrankungen in
    Handbuch der Neurologie (Lewandowsky) Berlin 1911 ii 694
Nonne, M   Arch f Psychiatrie, 1893 xxv Monatschr f Psychiatrie and
    Neurologie 1906 xx.
Putnam J J   A Group of Cases of System sclerosis of the Spinal Cord
    Associated with Diffuse Collateral Degeneration Occurring in En
    feebled Persons Past Middle Life and Especially in Women Studied
    with Particular Reference to Etiology Jour Nerv and Ment Dis. New
    York, 1891 xvi 69–110
Russel Colin K. Combined System Diseases of the Spinal Cord in Mod.
    Med (Osler and McCrae) 2d ed., Philadelphia and New York, 1915
    v 125–139
Russell J S. R. Batten, F E and Collier J Subacute Combined Degenera
    tion of the Spinal Cord Brain London 1900 xxiii 39–110

CLINIC OF DR. JULIUS FRIEDENWALD

Mercy Hospital

PERSONAL EXPERIENCE IN THE TREATMENT OF ULCER OF THE STOMACH

Brief Review of the Various Medical Methods of Treating Peptic Ulcer, The Leube Cure, the Lenhartz Cure, the Sippy Cure, Comparative Results of the Various Forms of Treatment, Einhorn's Duodenal Alimentation, Brief Discussion of the Surgical Treatment. Advantage of Pyloroplasty Over Gastroenterostomy. Method of Determining When an Ulcer Has Been Healed After Treatment.

SINCE Cruveilhier first advised an exclusive milk diet in the treatment of ulcer of the stomach, and Brinton first pointed out clearly the advantages of the rest treatment in this affection, much interest has been manifested by the medical profession in the treatment of this disease. Inasmuch as the etiology of this affection has not as yet been entirely satisfactorily established, many variations in treatment have been instituted, depending much on the individual views regarding its etiology. Rosenow's recent work has materially altered our views regarding the etiology of ulcer.

According to this investigator the cause of this disease is, in most instances, in all probability a hematogenous infection with special strains of streptococci absorbed from some focus of infection.

On this account the view is now generally maintained that previous to instituting treatment all sources of focal infection should as far as possible be removed. This infection may be dental, tonsillar, sinus, gall bladder, appendiceal, prostatic, or otherwise

Aside from removing all focal infections prophylactically, much can be done by means of a carefully selected diet in preventing the onset of ulcer of the stomach   As soon as the first symptoms appear the patient should be placed upon an exclusive milk diet   The temperature of the food should be regulated, so that it be given not too hot or too cold

Anemia, which so frequently accompanies this disease, must be combated   Hyperchlorhydria, which apparently bears some etiologic relation to this condition, must be overcome   There can be no question that healing is apparently prevented in some instances by the action of the acid gastric juice   This fact has been demonstrated by Sippy in his method of treatment of ulcer, in that by instituting neutralization of this gastric juice by the continued administration of alkalies the healing of peptic ulcers in many instances is established   Notwithstanding the fact that Hardt and Dragstedt have demonstrated that when peptic ulcers were produced by streptococci according to Rosenow's method without the presence of hyperacidity or that delayed healing may be maintained in spite of the absence of the digestive activity of the gastric juice, yet, clinically, hyperchlorhydria is usually observed in ulcer, as can readily be demonstrated by means of the Rehfuss method of fractional analysis

Again, if one takes the occasion to withdraw the contents of the stomach at the time the pain is at hand, one almost always finds in uncomplicated cases of gastric ulcer an excess of free hydrochloric acid   If no free hydrochloric acid is observed one cannot help but be suspicious of some complication or the presence of some other disease

Certain advances have been made in the medical treatment of peptic ulcer in the past few years   According to the older plan, the *Leube treatment* was almost constantly followed This consists of placing the patient at complete rest in bed for fourteen days or more upon liquid diet, mainly on milk   Upon such a diet the patient frequently loses much flesh as well as strength

On this account Lenhartz cautions against the strict ab-

stinence diet in the treatment of ulcer of the stomach, even in
those instances in which there is hemorrhage He bases his
conclusions on the fact that since ulcer of the stomach is most
frequently accompanied by superacidity and also by an en-
feebled condition, it is best to give protein food early to over-
come the acidity as well as to build up the system

In the *Lenhartz cure* absolute rest in bed for at least four
weeks is maintained An ice-bag is placed on the abdomen and
left on more or less continually for two weeks On the first
day, even though there be hematemesis, 200 c.c. of iced milk
are given in teaspoonful doses together with two raw ice-cold
beaten up eggs.

The eggs are beaten up with sugar, and they are kept cold
by placing the cup containing them in a dish filled with ice
The milk is increased every day 100 grams, and one additional
egg added, on the ninth day the patient is given 1 liter of milk
and the quantity is not increased, on the sixth day raw scraped
beef is added, and the quantity is doubled on the following day,
on the seventh and eighth days the patient is given some well
cooked rice and zwieback (softened), and on the tenth day raw
ham and butter

The Sippy Cure—More recently Sippy has evolved a
method of treating peptic ulcer which, according to our observa-
tion in a large number of cases, has yielded the most gratifying
results

Inasmuch as it is generally admitted that a peptic ulcer
heals if its surface is not continuously exposed to the digestive
action of the gastric juice, Sippy's treatment consists in protect-
ing the ulcer from the acid corrosion until it is healed by shield-
ing it from the corrosive effect of gastric secretion He ac-
complishes this by maintaining a neutralization of the free hy-
drochloric acid from early in the morning until late at night,
usually from 7 A. M. until 10 30 P M., or during the entire period
when food or gastric secretion is in the stomach.

If an excessive secretion is present at night this is removed
by aspiration, until the secretion has disappeared

The neutralization is effected by frequent feedings and

the administration of alkalies, given freely and at frequent intervals

Nourishment is given from the very onset of the treatment, preliminary starvation and administration of nutrient enemata, common to other forms of medical treatment, are of little value, according to Sippy   The patient remains in bed for three to four weeks   Three ounces of a mixture of equal parts of milk and cream are given every hour from 7 A M to 7 P M   After two or three days soft eggs and well-cooked cereals are gradually added until in ten days the patient receives 3 ounces of milk and cream mixture every hour, 3 or 4 boiled eggs, and 9 to 12 ounces of a cereal each day   Cream soups of various kinds, vegetable purées, and other soft foods may be substituted now and then as desired   One egg is given at a time, and 3 ounces of a cereal at a single feeding, the cereal being measured after it is prepared   The cereal and eggs are given alternately, and taken at the same time as the 3 ounces of mixture of milk and cream

The total bulk of each feeding should not be over 6 ounces After a longer or shorter period, according to the condition of the patient, a large variety of soft and palatable foods may be used, such as jellies, marmalades, custards, creams, etc   The basis of the diet, however, should be milk and cream, eggs, cereals, vegetable purées, and bread and butter   Alkalies are administered from the very beginning of the treatment between the feedings to neutralize the acid secretion, powders consisting of heavy calcined magnesia, 10 grains, with sodium bicarbonate, 10 grains, being alternated with powders of bismuth subcarbonate, 10 grains, and sodium bicarbonate, 10 grains   It is also advisable to give the powders every half-hour after the last night feeding for a number of doses

The after-management of these patients is important, the hourly feedings and alkaline powders must be continued even after the patient is pursuing his regular occupation   If for any special reason the hourly feedings cannot be maintained the three usual meals should be substituted, and the alkaline powders administered at frequent intervals

There can be no question but that a large proportion of ulcer

cases recover under medical treatment. According to our observations 72 per cent. by the Leube cure, 66 per cent by the Lenhartz cure, and 86 per cent. by the Sippy method   When an ulcer patient is treated medically he should be treated thoroughly, and ambulatory treatment is rarely advisable   As we have elsewhere shown, the results of ambulatory treatment is exceedingly unsatisfactory, inasmuch as in but from 40 to 50 per cent of cases so treated is a cure effected   I believe that many ulcer cases do not recover because treatment is not sufficiently prolonged. A rest cure of but a few weeks is often insufficient. In severe cases the patient should be put to bed for from six to eight and even more weeks

In those instances in which the ulcer is of a severe type, associated with excessive vomiting, pain, or with hematemesis, food should be withheld by mouth for three to five days, and the patient fed by rectum   A Murphy drip, consisting of normal salt solution and containing glucose, is especially to be recommended

Of the greatest importance in the treatment of certain cases of ulcer, especially those of a severe type accompanied by excessive vomiting and nausea, is the method devised by Einhorn, known as duodenal alimentation   By means of this method food can be introduced directly into the duodenum The instrument employed consists of a small capsule perforated and attached to a long rubber tube, at the other end of which a syringe can be applied   The tube is swallowed while drinking water, and the instrument soon passes into the stomach, and within an hour or two into the duodenum   Care should be taken to see that it is in place before the feeding is started This may be done by gentle traction, which shows a slight resistance if the tube is in the duodenum, by aspiration, which will often bring up golden yellow duodenal juice without any gastric secretion, or perhaps by giving the patient some liquid to drink by mouth and immediately performing aspiration. If the end of the tube is in the stomach, the fluid can be removed Any liquid food may be employed, but mixtures of milk, sugar, and raw eggs are the most useful   Care should be taken to see that there are no particles in the food that might clog the tube

The amount at the beginning should be small, 100 c.c. every two hours, beginning early in the morning and stopping late in the evening   This quantity may be gradually increased up to 300 c c   If eight feedings are given in twenty-four hours and each feeding consists of 280 c c of milk, 1 egg, and 1 tablespoonful of sugar of milk the patient will receive approximately 2280 calories, which is ample for an average individual, and if the patient is at rest in bed it is sufficient to allow a gain in weight.

Einhorn has perfected a special syringe with which it is possible to administer the food without disconnecting the tube. Morgan has suggested a method like that of Murphy for giving salt solution per rectum, permitting the fluid to flow from an irrigating jar, and so arranging the pet-cock that the food is taken slowly, the 300 c c of nourishment taking about twenty-five minutes   The food should be administered at body temperature and the heating should be done slowly, for if it becomes too hot it is liable to become thick and lumpy   After heating, it is well to strain the food to be certain to have it free from small particles   If the food is administered too warm or too cold it is apt to cause uncomfortable symptoms, sometimes causing the patient considerable shock, a too rapid administration causes flatulence   After each feeding a syringeful of water at 93° F should be injected, then the pet-cock closed and the syringe filled with air, which should be injected after the pet-cock has been again opened, the pet-cock should then be closed and the syringe disconnected   The procedure is very important and serves to keep the tube clean and empty   The tube is left *in situ* for about ten days, after which it may be withdrawn

Of the remedies employed in the treatment of peptic ulcer there is one of unusual importance, as it appears to have an almost specific effect in some instances   The drug is atropin, which by depressing the vagus fibers decreases the secretory and motor functions of the stomach   Through the researches of Eppinger and Hess the theory has been advanced that disturbances of the autonomic nervous system (which includes all of the efferent nerve-fivers outside of the cerebrospinal axis ex-

cepting those supplying the voluntary muscles) lead to increased and decreased tonus or excitability, and that through this system the activity of the glands of internal secretion are regulated and controlled   According to this theory, therefore, a gastric ulcer may have as its underlying basis an increased vago-tonus, and atropin by depressing this vagus excitability decreases the possibility of gastric irritation   Clinically it has frequently been noted that healing has been effected in obstinate cases of gastric ulcers when patients were systematically treated with atropin or belladonna

Scarlet red, too, is a useful adjuvant according to our experience in the treatment of peptic ulcer, and while it cannot by any means replace the usual forms of treatment when administered in conjunction with them, it adds materially to the effectiveness of the cure   It is of great help when administered in the ambulatory cases, the effect being even more favorable than the usual remedies, such as bismuth   Inasmuch as scarlet red in no way interferes with the administration of other remedies, such as the alkalies or atropin, these may be administered when indicated at the same time, and, in fact, the effect of the combination is at times most beneficial.

THE SURGICAL TREATMENT OF PEPTIC ULCER

Simple uncomplicated gastric and duodenal ulcers do not require operation   Operation must only be considered when there are complications or when the ulcer has resisted a thorough medical treatment, especially is operation indicated in those cases accompanied by severe and persistent pain, vomiting or hemorrhage or in pyloric and duodenal ulcers accompanied by stenosis   In ulcers situated at other parts of the stomach operation gives but slight relief unless radical procedures (resection or excision) are undertaken   Operation should be promptly practised in all cases of perforation, and ulcers of the stomach accompanied by tumor formation always demand surgical intervention

The character of the surgical procedure to be selected is of the greatest importance   This, of course must vary according

to the situation and extent of the ulcer, thus the good effect of gastro-enterostomy is dependent upon the proximity of the ulcer at the pylorus, the closer to the pylorus, the better is the prognosis According to Finney and myself the results of pyloroplasty and pylorectomy are far better than gastro-enterostomy In a comparison of 100 cases of pyloroplasty with a similar number of cases of gastro-enterostomy the following conclusions were drawn by us

1 The operation of pyloroplasty has its greatest indications in the relief of pyloric stenosis due to chronic ulcers situated at or near the pylorus, and on either side of it or resulting from cicatricial contraction following the healing of such ulcers It is often a useful procedure in cases of hemorrhage due to gastric ulcer on the lesser curvature or to duodenal ulcers which cannot be controlled medically, and which threaten the life of the patient, as well as in chronic dyspepsias due to ulcers which have not been relieved by medical treatment

3 The operation has certain advantages over gastro-enterostomy and but few of its disadvantages

3 Such objections as are urged against the operation— e g , its inapplicability in the presence of adhesions surrounding the pylorus as well as in the presence of active and bleeding ulcers, and also because of the fact that the new opening is not at the lowest point taking advantage of gravity—are, according to our experience, more fanciful than real, since the operation has frequently been performed under these conditions with most gratifying results

4 The only contraindications to the operation are inability to mobilize the duodenum when adhesions are too dense and thickening and infiltration about the pylorus due to hypertropic forms of ulcerations These conditions, however, in our experience occur but rarely

5 The special advantage of this procedure lies in its affording the opportunity to excise all ulcers in the anterior wall of the stomach or duodenum after direct inspection of the parts affected, also the application of treatment to ulcers situated in the posterior walls It does not greatly disturb the normal

relation between the stomach and intestines, as one finds after pylorectomy or gastro-enterostomy

From our experience with pyloroplasty the immediate as well as the final results are most encouraging While in some instances gastro-enterostomy may be the operation of choice, nevertheless we believe that on account of its comparative unsatisfactory end results it should as far as possible be limited to the relief of stenosis of the pylorus due to malignant disease, and that usually in nearly all other conditions pyloroplasty and pylorectomy are safer and more satisfactory procedures

According to our observations there were 90 per cent of immediately successful recoveries and 86 6 per cent of satisfactory end results following pyloroplasty, while there were but 82 per cent of satisfactory immediate recoveries and 77 2 per cent of satisfactory end results following gastro enterostomy

I feel that a word must be said regarding the question as to whether an ulcer has really healed aside from the fact as is indicated by the relief of symptoms Baetjer and I were among the first to call attention to the fact, and other clinicians have since corroborated this finding that the degree of healing can be determined by means of the x ray In ulcer, when the patient is given a rest-cure treatment, all symptoms gradually disappear, and the patient becomes, comparatively speaking, well This usually takes place in from four to five weeks At the end of this time, however, if a second bismuth examination is made, we often find the same characteristic signs as in the first ulcer, though the patient shows no symptoms whatever In a series of ulcer cases that have been examined, in from three to four weeks after an absence of symptoms we have frequently found but little change in the defect or motility of the stomach

When these patients are given the ordinary diet these symptoms may recur in a short time If treatment is continued, however, our experience has demonstrated that as the ulcer continues to heal the motility of the stomach returns to a more normal condition, and by making repeated x ray observations over a long period of time we can observe when the ulcer has

healed, and we are thus enabled to determine the progress of healing This method has been utilized to great advantage by us in many instances

I cannot conclude the treatment of ulcer without drawing attention briefly to the after-treatment of this affection

There can be no question but that relapses are frequently due to indiscretions in diet following the cure when the patient is no longer under the control of his physician The patient should be placed upon a carefully regulated diet free from acids and indigestible food, intermediate feedings should be prescribed and alkalies be given for some months following the cure When possible it is my habit to have my patients report for re-examinations at periods of three to four months for a year or more, so as to determine the ultimate result of the treatment I am presenting a diet list which my patients follow as an after-treatment

DIET LIST FOLLOWING AN ULCER TREATMENT

In addition to the usual meals intermediate feedings should be taken

MAY TAKE

Soups	*Meats (minced)*	*Poultry*	*Bread*
Clam	Boiled	Boiled	Stale
Mutton	Broiled	Broiled	Toasted
Barley	Lamb	Roasted	Pulled
Rice	Lamb chops	Chicken	Wheat
Vermicelli	Mutton	Turkey	Zwieback
Cream	Mutton chops	Squab	Crackers
Potato	Brains		
Pea	Sweet-breads		
Celery			
Asparagus			

Fish (minced)	*Eggs*	*Milk*	*Butter*
Boiled	Raw	Whole	Vegetables
Baked	Soft boiled	Skimmed	Asparagus
Broiled	Poached	Whey	Spinach
Blue fish	Omelet	Curd	*Cauliflower*
Bass	Scrambled	Junket	Squash
Haddock	Shirred	Matzoon	Watercress
Halibut		Kumiss	Potatoes
Trout	*Cereals*	Kefir	Mashed
Mackerel	Rice	Cream	Baked

Fish (minced)
Oysters
  Raw
  Steamed
  Stewed
  Broiled
Clams
  Broth
  Raw
  Steamed

Farinaceous Food
Cornstarch
Tapioca
Sago
Vermicelli

Cereals
Cracked wheat
Cornmeal
Barley
Oatmeal
Cream of wheat
Farina
Hominy
Grits
Shredded wheat

Fruits
Pears
  Stewed
Peaches
  Stewed
Prunes
Apples
  Stewed
  Baked

Milk
Pasteurized
Buttermilk

Ice-cream
Vanilla

Beverages
Barley water
Oatmeal water
Rice water
Albumin water
Tea (weak)
Coffee
Cocoa

Mineral Waters
Vichy
Hawthorne
Lithia
Apollinaris
White Rock
Poland

Butter
Carrots
Artichoke
Lima beans
Lentils
Peas
String beans

Desserts
Puddings
Rice
Blanc mange
Cornstarch
Bread
Tapioca
Cup custard

ARTICLES OF DIET TO BE FORBIDDEN

Candies
Salads
Fried foods
Alcoholic stimulants
Sweet potatoes
Strong tea
Strong coffee
Cabbage
Salted fish
Smoked fish
Sardines
Salmon
Preserved fish
Beef
Pork
Veal
Crabs
Rich soups
Liver
Kidneys
Duck
Corn

Goose
Potted meats
Corned meats
Stews
Hashes
Sausage
Twice cooked meats
Celery
Beets
Radishes
Hot cakes
Hot bread
Berries
Bananas
Melons
Oranges
Grape-fruit
Lemons
Preserves
Pastry
Pies
Nuts
Tomatoes

The following diet presents our method of feeding during the Sippy Cure. Either sodium bicarbonate with magnesium calcined or sodium bicarbonate with bismuth subcarbonate are given alternately every hour on the half-hour from 7 30 A M to 10 30 P M

Hour A M	Days 1st to 5th	Sixth	7th to 8th	9th to 10th	11th to 14th
7	Milk and cream	Soft egg Milk and cream	Milk and cream	Cereal Milk and cream	Soft egg Cereal Milk and cream
8	Milk and cream	Milk and cream	Milk and cream Soft egg	Milk and cream	Milk and cream
9	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
10	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
11	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
12	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
P M 1	Milk and cream	Milk and cream	Soft egg Cereal Milk and cream	Cereal Egg Cocoa	Egg Cocoa Custard
2	Milk and cream	Milk and cream	Soft egg Milk and cream	Milk and cream	Milk and cream
3	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
4	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
5	Milk and cream	Milk or cocoa Soft egg	Cereal Milk and cream	Milk toast Egg and cocoa	Milk toast Egg and cocoa
6	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
7	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream

Milk and cream each 1½ ounces

Hours A.M	Days 15th	16th	17th to 18th	19th
7	Egg cereal	Egg cereal	Soft egg	Milk and
	Milk and	Milk and	Cereal	cream
	cream	cream	Cocoa	
8	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
9	Milk and	Milk and	Milk and	Chicken
	cream	cream	cream	broth
10	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
11	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
12	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
P.M. 2	eggs	Egg milk	Minced	Minced
	cocoa	Cream-milk	chicken	chicken
1	Milk toast	Toast	Milk	Cocoa
		Vanilla Ice-cream	Milk toast	Dry toast
			Vanilla Ice-cream	Vanilla Ice-cream
2	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
3	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
4	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
5	Milk toast	Milk toast	Milk toast	Milk toast
	Egg cocoa	Egg cocoa	Egg cocoa	Egg cocoa
6	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
7	Milk and	Milk and	Milk and	Milk and
	cream	cream	cream	cream
		Milk and cream 1½ ounces		

Hours A.M	Days 20th	21st.	22d or
7	2 eggs	2 eggs	Milk and cream
	Cocoa	1 slice toast	
	1 slice dry toast	Butter	
	Butter		
8	Milk and cream	Milk and cream	Milk and cream
9	Milk and cream	Milk and cream	Cereal
	Egg	Egg	Milk and cream
			Egg
10	Milk and cream	Milk and cream	Milk and cream
11	Broth	Milk and cream	Milk and cream
12	Milk and cream	Milk and cream	Milk and cream
			Milk and cream

Hours	Days		
	20th	*21st*	*22d on*
P M 1	Minced chicken 1 slice dry toast Butter Cocoa Spinach	1 Lamb or mutton Chop broiled Dry toast Cocoa Butter Asparagus or baked potato	Chop or minced chicken Dry toast Strained vegetable or baked potato Cocoa Butter
2	Milk and cream	Milk and cream	Milk and cream
3	Broth	Milk and cream or milk and egg	Milk and cream
4	Milk and cream	Milk and cream	Milk and cream
5	2 eggs Cereal Milk toast Cocoa	2 eggs Cereal Milk toast Cocoa	Stewed fruit or baked apple 2 eggs Cereal Milk toast Cocoa
6	Milk and cream	Milk and cream	Milk and cream
7	Milk and cream	Milk and cream	Milk and cream

Milk and cream each 1½ ounces

Modified Sippy Diet followed in some cases of peptic ulcer

MILK AND CREAM, EQUAL PARTS, 1½ OUNCES EVERY HOUR FROM 7 A. M TO 7 P M, NINE TO TWELVE DAYS

A. M	P M.	Medicines	
7 30	1 30	Heavy calcined magnesia	gr x.
9 30	3 30–5 30	Sodium bicarbonate	gr x
11 30	7 30–9 30		
A. M.	P M.		
8 30	12 30– 2 30	Bismuth subcarbonate	gr x
10 30	4 30– 6 30	Sodium bicarbonate	gr xx
	8 30–10 30		

THREE TO FOUR DAYS FOLLOWING

A M	P M		
7	3	Milk and cream	88 oz. 188.
11	7		
A. M.	P M		
9	1 and 5	Milk and egg or cocoa	
A M	P M	Medicines	
7 30	3 30	Heavy calcined magnesia	gr x.
11 30	7 30	Soda bicarbonate	gr x.
9 30	1 30	Bismuth subcarbonate	gr x.
	5 30	Soda bicarbonate	gr x
	9 30		

Four to Five Days Following

A. M.	P M.		
7–11	3–7	Milk and cream	44 oz. iss
9		Oat meal, egg and cocoa.	
	P M.		
	1 and 5	Milk toast, egg and cocoa	
		Medicines	
A M	P M.		
7.30	3.30	} Heavy calcined magnesia	gr x.
11.30	7.30	} Sodium bicarbonate	gr x.
A M.	P M.		
9 30	1 30		
	5 30	} Bismuth subcarbonate	gr x.
	9.30	} Sodium bicarbonate	gr x.

To be Followed for Several Weeks

A. M.	P M.		
7	3–7	Milk and cream	44 oz. iss.
11		Milk and egg or cocoa	
9	1–5	Soft diet without acids.	
A. M.	P M.		
7.30	3.30	} Heavy calcined magnesia	gr x.
11 30	7.30	} Sodium bicarbonate	gr x.
A M.	P M.		
9 30	1.30		
	5.30	} Bismuth subcarbonate	gr x.
	9 30	} Sodium bicarbonate	gr x.

As required additional sodium bicarbonate.   gr x to xx.

VARIOUS TYPES OF ACHYLIA GASTRICA AS REVEALED BY THE REHFUSS METHOD OF FRACTIONAL ANALYSIS

IN the study of the gastric secretion important knowledge has been obtained by means of the Rehfuss method of fractional analysis According to this method, the gastric function is investigated by examining small amounts of secretion extracted at frequent intervals after a test-meal by means of the Rehfuss tube This method has so materially altered our views regarding the variations in gastric acidity that it has become necessary to revise the results of our former analyses both in health and disease One soon learns from this method of investigation that an analysis of the gastric contents at the end of an hour is by no means sufficient to allow us to draw conclusions as to the degree of acidity which may exist in any particular gastric disorder, for whether there be either a hyperchlorhydria or a hypochlorhydria at hand, the gastric secretion may not have risen to its height at the end of an hour, or may have done so before this time, and thus many phases of the hyperacidity or hypo-acidity may be entirely overlooked

ourselves that these are spurious achylias and that the acid was present before or after the hour

In order, therefore, to differentiate between the true and spurious achylias it is necessary to study every case of achylia gastrica by means of a fractional analysis

In our series of achylias fractional analyses were made in 41 instances   These cases were all true achylias, in which no free hydrochloric acid was secreted during the entire period of digestion, no false or spurious forms have been included in this group

Of the 41 cases, there were 15 of simple achylia, 4 of chronic gastritis, 3 of gastric ulcer, 7 of carcinoma of the stomach, 3 of pernicious anemia, 2 of cholelithiasis, 2 of pulmonary tuberculosis, 2 of syphilis of the stomach, 2 cases following pylorectomy, and one case following gastro-enterostomy   In addition to these cases there were 37 cases of spurious or false achylias which cannot be properly included in this list   A number of these false achylia cases presented an excess of free HCl at the end of one and three-quarter to one and one-half hours, in several instances of 70 or 75, and were thus really cases of delayed hyperacidity   Rehfuss has called attention to the distinction between psychic achylia in which there is a suppression of the secretion during the first stage of digestion and a chemical achylia, a total absence of both secretions would indicate a complete achylia

In the simple achylias, in addition to the fact that free HCl is absent in every specimen, the total acidity is observed to be very low, rarely reaching above 10 to 15   In the fasting stomach there is none or but little gastric secretion, and the stomach is empty within two hours, usually between one and one-half and one and three-quarter hours   The ferments are absent or are much diminished   Blood is occasionally found in these cases, sometimes visible, sometimes occult   This is due, as Anderson points out, to the friable state of the gastric mucosa in this disorder, which is very apt to bleed   Bile is frequently regurgitated into the stomach during the early period of digestion, and is often found at the end of twenty to thirty minutes

In the group of cases of chronic gastritis the same character-
istics were observed as one usually finds in simple achylias
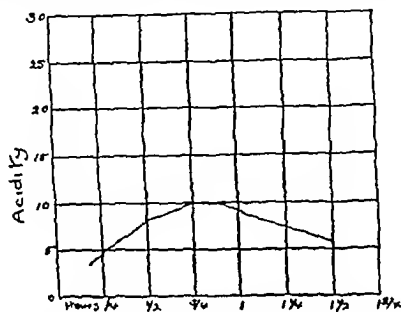
Fig. 283—Fractional analysis in a case of simple achylia gastrica.

The total acidity is usually higher, sometimes as high as 40
during the period of digestion, in addition, mucus is obtained
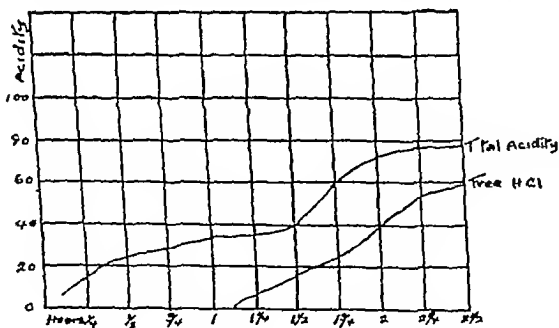
Fig. 284—Case of delayed gastric digestion or spurious achylia.

in almost every specimen, which is not frequently observed in
simple achylia   The motility of the stomach is usually delayed

In 3 of our cases of peptic ulcer there was a true achylia, in none of which was there any free HCl at any time during the entire period of digestion   These cases represent an interesting group which tends to offset the claim of Sippy and others that peptic ulcer is largely dependent for its formation upon the corrosive effect of the acid gastric secretion   However, this condition occurs according to our experience in but so small a proportion of cases that it alone cannot be accepted as definite proof in this regard

There are 7 cases of gastric carcinoma in our group   The quantities of gastric secretion obtained varies in this condition according to whether there is or is not a pyloric obstruction at hand   In the non-obstructive cases there is a very rapid emptying of the stomach, while in the obstructive forms there is marked retention

The total acidity varies much in these cases   In 2 the total acidity remained at 10 or below, while in the remaining 5 cases it was much higher in certain specimens 25 in one, 32 in another, and 43, 52, and 54 in others   In these specimens presenting a high total acidity lactic acid is usually present   Blood is frequently present in the specimens and may appear at any time during the period of digestion, mucus is usually abundant. The Wolff-Junghans reaction is positive and the protein curve diverges quickly from the acid curve, considerable amounts of albumin being usually present within three-quarters of an hour, the quantities being markedly increased to positive reactions within an hour or an hour and a half

The pernicious anemia cases present the typical features of the true achylias   The fasting stomach contains but a small amount of contents   The total acidity is low, usually below 15, and the stomach is emptied rapidly

In 2 of our cases of cholelithiasis there were true achylias The total acidity was as high as 25 and 40 in these cases and the stomach emptied itself rapidly

In the 2 cases of pulmonary tuberculosis there was a true achylia   The total acidity was low and the stomach was emptied within one and one-quarter hours in both instances

The 2 cases of gastric syphilis are interesting inasmuch as they presented conditions similar, in respect to the gastric secretion, to those found in carcinoma. The total acidity reached 42 and 56 respectively, the stomach emptying itself rapidly

In the 2 operated cases (gastro-enterostomies) there was a marked delay in the emptying of the stomach, while in the pylorectomy case there was a hypermotility, in all 3 there was constantly a fairly low total acidity, and the specimens contained bile and mucus

CONCLUSIONS

1 Fractional analysis of the gastric secretion according to the Rehfuss method is extremely important in all cases of achylia gastrica, inasmuch as by means of this method one can easily differentiate the true achylias from the spurious forms   This differentiation is extremely important, inasmuch as many of the false achylias present a very high HCl acid index, sometimes marked hyperacidity, and are, in fact, really cases of delayed hyperacidity

2 In the true achylias free HCl is absent in every specimen, the total acidity is low and there is a marked hypermotility

3 In the form of chronic gastritis associated with achylia there is a high or low total acidity, considerable mucus in almost every specimen, and there is usually delayed motility

4 In most instances of gastric carcinoma one finds a typical achylia, frequently with delayed motility, and a rather high total acidity and with lactic acid and blood The Wolff-Junghans test is positive, considerable amounts of albumin being present within three-quarters of an hour, being markedly increased within an hour to an hour and a half

5 In pernicious anemia one observes the typical features of a true achylia There is a low acidity and the motility of the stomach is rapid

CONTRIBUTION BY DR. JOHN RUHRÄH

UNIVERSITY OF MARYLAND

SOME OF THE ASPECTS OF EPIDEMIC INFLUENZA IN CHILDREN

THE devastating epidemic of influenza, with which we are all familiar, affected children almost as much as adults, but, fortunately, the cases were, as a rule, light and the mortality low While this is true, the epidemic presented a large number of rather unusual clinical pictures, to some of which I wish to call your attention today Among the noticeable features of the disease were certain changes in the eyes. These were usually slight, consisting of a moderate grade of conjunctivitis which lasted from one to three days or more, accompanied generally with a slight degree of photophobia Occasionally the photophobia was so intense as to suggest meningitis, the child turning away from the light and burying its head in the pillows and objecting bitterly to having its eyes examined in the bright light. Certain other cases, as in the case presented to you, showed a certain amount of edema, especially of the upper eyelids of either one or both eyes, and this was generally attended with a decided pinkish color, which calls to mind the epidemic form of conjunctivitis, commonly known under the name of "pink-eye" Occasionally there was involvement of the ocular conjunctivæ, sometimes only of one eye or only of part of it. All of these eye symptoms subsided promptly, the only treatment being necessary was an antiseptic eye wash of 1 grain of boric acid and 1 dram of camphor water and enough distilled water to make 1 ounce In one or two instances it was noted that the conjunctivitis showed a definite tendency to persist,

but these cases responded promptly to an astringent, such as 1 grain of sulphate of zinc in 1 ounce of distilled water

The second group of cases shows you three patients with middle-ear affections, one each of the three commonest affections of that organ during the epidemic In the early part of the epidemic there were but very few ear complications among children, but later on there were quite a number of cases of inflammation The first child has a marked earache, with a very red throat and only a slight injection of the vessels running along the hammer and a little redness at the upper part of the drum The second child has a decidedly red drum, but with no evidence of any fluid in the middle ear, but has been suffering a considerable amount of pain The third child has not only a reddened drum, but bulging, slight deafness with considerable discomfort, and had earache at the onset, but this has very largely disappeared The first 2 cases will probably be relieved by phenol and glycerin, 25 grains to 1 ounce, instilled at four-hour intervals The last case should be opened with a free incision

Not only have there been comparatively few ear complications but also very few involvements of the mastoid, which, if I am correctly informed, is quite different from the epidemic of 1889-90

You will note that one of these children has a decided hoarseness, with a barking, croupy cough This patient may serve as a text for a few words on the subject of laryngeal complications in influenza which, while not very frequent, have been exceedingly troublesome Most of the cases have come on after the attack has been well established, although occasionally the larynx has been involved from the onset Most of the cases have not been very severe and have not required anything more than the measures usually employed in mild cases of laryngitis I have, however, seen two instances in which intubation had to be done One of these children was suffering with nephritis which it had had for many months, and there was some tendency to edema The onset of the influenza was in the usual manner, but after two days there was a very marked bronchitis and involvement of the larynx producing attacks not unlike catarrhal

spasm, but there was no relaxation in the dyspnea between the spells   The child's voice was not entirely lost, but the dyspnea became so marked that it required an intubation to relieve it   This patient eventually recovered

The second case occurred in a patient who had influenza complicated with a severe bronchopneumonia. The child became very hoarse, the dyspnea much more marked than the lung involvement would seem to warrant, and gradually the voice was practically lost   There was marked cyanosis and very labored respiration, all of the accessory respiratory muscles being brought into play   The child was intubated and had two days of comparative relief, when the dyspnea again became more or less marked and a very marked toxemia set in, which proved fatal after twenty four hours' duration   In the second instance the later dyspnea seemed to be due to the extension of the pneumonia and the failing heart.

In addition to these cases, there have been a number of others of a similar nature under the care of other physicians   In these cases of influenzal laryngitis it seems to me to be good practice to have an intubation done as soon as the dyspnea becomes severe enough to bring into play the accessory muscles of respiration, for even if the condition of the child is not very alarming it relieves the heart strain and fatigue incident to forced respiration

The nose and throat in influenza are worthy of a word   In practically every case there is a more or less marked angina, the inflammation extending over the entire pharynx, tonsils, soft palate, all of these tissues being swollen, reddened, and in some there was a certain amount of pain on swallowing and tenderness on palpating the sides of the neck   In most instances the inflammation extended over the hard palate to the cheeks, but there was nothing that could be called a pathognomonic enanthem   Small punctate hemorrhages were common   The inflammation in the pharynx had a tendency to spread downward, causing a tracheitis and bronchitis, and to spread up through the nose, so that in one or two or three days there was more or less evidence of coryza, but this in children varied a great deal

In some the nose was dry throughout the entire course of the disease In other cases there was a rhinitis with a marked purulent discharge from the onset, while in others the discharge did not begin until the second or third day, and consisted chiefly of a more or less clear fluid and had a tendency to excoriate the lip and the skin about the nose In very young children the rhinitis produced a very considerable amount of discomfort, interfering markedly with nursing and causing mouth breathing

The nasal condition was treated according to the local conditions, one-half strength Dobell's solution generally being employed for the milder cases, and 10 per cent argyrol solution for those that were more severe, and where the secretion was thick and tended to dry in the nose, 5 per cent solution of bicarbonate of soda followed by the use of 5 drops of eucalyptol and 1 ounce of liquid petrolatum afforded considerable relief In a few instances in order to allow the proper instillation of the various medicaments employed a 1 10,000 solution of adrenalin chlorid was used a few minutes before the treatment This resulted in shrinking back the mucous membrane so that there was no difficulty in cleansing the nose

Involvement of the sinuses in children was, in my experience, very rare, certainly nothing beyond what cleared up in the course of the disease without any attention being paid to it

The odor of the breath was very striking, so that the diagnosis could almost be made on entering the room This was more marked in some cases than in others, but practically never absent Where several children were sick in the same room the air became exceedingly disagreeable in spite of good ventilation The odor is difficult to describe, but not unlike that caused by a decaying human cadaver

In practically all cases there was sooner or later more or less bronchitis In a certain proportion of cases, although not a very large one, a pneumonia developed In young infants this was a bronchopneumonia not differing very much from the types ordinarily seen, except there was probably a greater tendency to cyanosis and extreme prostration In older children the pneumonia was very often of the bronchial type similar to that

seen in adults, but in some instances it was definitely lobar, at least as far as the clinical picture went   These older cases tended, as a rule, to clear up, but were very frequently complicated by pleural effusions   In some cases the effusion was purulent and a more or less creamy pus of the ordinary empyema being encountered, and these cases were best treated by the usual procedure of drainage   Occasionally a thin pus or what is called "dish water" pus was encountered, and these cases did very badly without regard to the form of treatment employed, and in a large number of cases the effusion was of a straw color, but contained a considerable amount of pus as shown under the microscope   In these cases the recovery was usually rapid, and the cases which cleared up quickly before it was thought necessary to do a puncture for diagnosis were supposed to have been of this type

In others the symptoms were very severe, the child being profoundly ill, with a high septic temperature and generally, but not always, a marked leukocytosis   In these cases it often sufficed merely to draw off an ounce or so of fluid for diagnostic purposes and the remainder was rapidly absorbed   In 3 cases there were very severe symptoms which disappeared within forty-eight hours after the puncture and in two of these there was a marked meningismus, so much so that the diagnosis of meningitis had been made on the clinical findings, but all of the nervous symptoms promptly abated with the rapid recovery of the child   In one or two instances where the pneumonia of the lobar type was unduly prolonged and an empyema suspected, the mere puncture by the exploratory needle seemed in some way to stimulate the inflammatory processes, as almost immediate recovery followed even though no fluid could be found

Taken all in all the outlook in the pneumonic cases in children was very much better than similar cases in grown people   Leaving out the deaths from bronchopneumonia in young infants, the fatalities were comparatively few

The skin manifestations of influenza are extremely interesting and can be described under several headings   Almost all cases showed a marked flushing of the face   This was a curious

reddish-purple blush over both cheeks, sometimes over the entire face and neck, and there was a certain amount of congestion, sometimes being of a very decided purplish color, at other times the red predominated This flushing was so constant in children that it can be regarded as a very valuable diagnostic sign Over the remainder of the body there was more or less congestion, so that the skin paled on pressure, sometimes there was just enough to produce a slight flushing of the skin, at other times, especially in the severer cases, there was a decided stasis of the superficial circulation, and when coupled with heart failure gave the skin an ash-gray-purplish appearance such as is seen in dying persons Curiously enough, the congestion, while generally of some prognostic importance, was not entirely reliable, as many cases showing marked changes in the skin circulation made a perfectly good recovery

In addition to the circulatory changes there were several types of skin eruptions seen, none of which could be regarded as pathognomonic The most significant, which was apparently more often noted in children than in adults, resembled the rose spots seen in typhoid fever These spots were very variable as regards number and most frequent on the chest, abdomen, and back, and sometimes are noted on the extremities and occasionally even on the face In one or two instances they were so numerous as to lead to a lay diagnosis of measles These spots are probably due to invasion of the skin by the influenza virus, whatever that may be, and are similar to the spots in typhoid, to the spots seen in colon bacillus infections, and in certain forms of tuberculosis There was a very considerable amount of vasomotor disturbance in the skin, so that handling produced spots of redness, and in some cases there were small areas of an urticarial-like eruption

The gastro-intestinal tract was involved in a great many cases In a certain number the disease began with vomiting, sometimes there were only one or two vomiting attacks, after which the stomach remained quiet In others the vomiting was severe and continuous and very much like that seen in recurrent vomiting Some of these children developed a very marked odor

o the breath, and some of them more or less acidosis, with great
rostration and somnolence   In other cases the vomiting was
rought on by attempting to feed the child more than he wanted
o take   Almost from the beginning of the epidemic it was
ealized that there was danger of producing vomiting and
iarrhea if the child was improperly fed, so that strict directions
were left in every instance to give the child plenty of water, small
amounts of bicarbonate of soda, either in water or milk, and the
only foods allowed were diluted milk, very thoroughly cooked
cereals, and a little orange juice   The food was ordered at
three-or four hour intervals, and instructions left to allow the
child to take what it wanted, and then wait until the next feeding
time without attempting to force it to take more   Where the
child was taking very little food, the amount of fluid given,
either in the form of water or diluted orange juice, was re-
garded as important, and this was given in small quantities at
rather frequent intervals   Where this plan was followed there
were very few cases of vomiting or diarrhea apart from those
that came on at the onset of the disease   In a few there was a
very marked intractable diarrhea with thin watery stools and
marked tenesmus   Many of these patients complained of ab
dominal pain and a certain amount of general abdominal ten
derness   These patients usually recovered in a few days

The temperature charts which I present for your consideration
show several different types, all of which were frequently
met with   In most of the cases in children under fifteen the
temperature was highest at the onset, gradually became lower, and
usually reached normal by the end of three days   This led to
the term "three-day fever"   In others the temperature per-
sisted for five or six days, gradually reaching normal, and oc-
casionally the febrile period was prolonged well into the second
week, although most of these cases in which there was a pro-
longed elevation of the temperature showed some complication
to account for it. In other cases the temperature reached
normal on the third day, remained down for a day or two, and
then recurred for two or three more days, when the normal
point was again reached   In almost every instance in which the

child was allowed to be up on the day following the fever and especially if any very marked amount of physical exercise was indulged in there was an immediate return of the fever and other symptoms, and this led to the practice of keeping the children in bed until forty-eight hours free from fever had elapsed, and then allowing them to sit in a chair for half an hour to an hour, gradually increasing the time each day, but carefully guarding against exposure and exercise   In a very large number of cases the temperature became subnormal for two or three days, and the same plan was practised with these cases   In every case where the rule was broken there was a recurrence of fever and of symptoms

After the first remission of temperature, when the normal point was again reached, any further rise was taken to mean some complicating inflammation, and in all cases where the tempera ture was unduly prolonged a careful search was made to find an explanation for it, but there were some instances in which this apparently occurred in an uncomplicated form of the disease

The fatal cases were, for the most part, either due to pul monary complications, as noted above, or to a very severe general infection   In these latter cases the child was taken suddenly ill, usually with a very high temperature, 105° to 107° F   At the beginning the child was exceedingly irritable and delirious, but soon passed into a more or less comatose condi tion   There was marked cyanosis of the entire body, and while the heart remained strong, there was a purplish flush of the skin, and as the heart weakened this became the ash-gray color of the moribund   The breathing in these cases was generally not much increased in rate, but at the same time the child seemed to have difficulty in getting the air into and out of the lungs, so that the accessory muscles of respiration were called into play   There was some discharge from the nose, a reddened throat, vomiting if attempts were made to give food or fluid, and generally a diarrhea   The patient sank rapidly, heart stimulants having no effect whatever, and death generally took place within forty-eight hours of the onset   These cases had little to differentiate them from the malignant cases of other infectious diseases unless it was the intense cyanosis

CLINIC OF DR GORDON WILSON

MEDICAL DEPARTMENT UNIVERSITY OF MARYLAND

FUNDAMENTALS IN THE TREATMENT OF PULMONARY TUBERCULOSIS[1]

THE successful treatment of this disease depends almost entirely upon the physician's accurate knowledge of the disease and his patient, and the patient's thorough co-operation and faith in his doctor

A diagnosis having been established, the doctor must bear in mind that he is treating an *acute exacerbation of a chronic disease*, and that his duty does not end in getting his patients free of symptoms and restored to apparent health, unless he has taught them (1) that the disease is a chronic one and frequently has long periods when symptoms are absent, (2) that the beginning of an exacerbation is accompanied by symptoms so slight that they may be overlooked, unless watched for, (3) that the "lunger," more than most people, must have a "reserve in health" upon which he can "draw" when needed, and, (4) that the one who remains well is the one who does not believe himself "cured," but knows that he is only "arrested," and lives accordingly

In breaking the news to your patient that he has tuberculosis, you must remember that to nine out of ten people this means an incurable disease, and no one willingly believes that his case is incurable Unless you can make your patient believe that he has tuberculosis, and that tuberculosis is curable, you will have failed in the first essential toward a cure, as ordinarily the patient responds so quickly to a rest cure that he begins to doubt that he has anything so awful as consumption," since he is "getting well so rapidly "

To the physician, who would start his patient right, the time spent in announcing his diagnosis and giving advice should not be considered unimportant or gone over rapidly, and I believe that more lives have been prolonged or saved by an hour expended at this time, than through an additional month spent later in the "cure" In carrying out this first essential you will, therefore, have to make your patient know and *believe* that he has a "curable" disease, and to do this, it is not enough to state it as a fact, but you must cite examples of persons in his community, known to him, who have had tuberculosis, and who have lived apparently normal lives, or cite such men as Trudeau, who have lived their allotted span and accomplished much. There are very few communities in which there does not live at least one apparently healthy man who "had a hemorrhage when he was young" In driving this fact home don't forget another trait of human nature, namely, that all of us believe more readily "the printed than the spoken word" (as exemplified by the sale of patent medicines by advertisements), and on that account show them in your books that practically no one who has reached the age of fifty fails to show in his lungs, if examined after death, the scars at least of a tubercular infection, no matter what might have been the immediate cause of his death, or whether he had ever been sick in his life prior to his fatal illness In making your diagnosis known, and in trying to make it be believed, don't hesitate, if necessary to explain to your patient how you arrived at your diagnosis, in other words, why you think he has "Tb" One failing of our profession is the belief that the lay mind is incapable of understanding medical matters, forgetting that we ourselves when medical students had just such minds, but have been made to understand Not infrequently I have realized that I have not succeeded in making my patient really know that he has tuberculosis, and in such cases I have urged that he see some other *lung specialist*, naming to him a number, so that he will know that I am not referring him to a single man who will "back up" my diagnosis through "medical ethics," a belief by the laity as to "medical ethics" which is somewhat prevalent

Having accomplished the first essential in making your patient *believe*, the second step follows naturally, and that is for him to make "his confession of faith" and acknowledge to the world that he has tuberculosis by going to a sanatorium, or health resort, that stamps him with the "stigma" Most of the real good, at least of the permanent type, is accomplished after the patient leaves the sanatorium, and is in a great measure due to the fact that he is not ashamed to own up that he has (or has had) tuberculosis, and can live the proper life, while the man who has failed to make "his confession of faith" is always hiding the fact of what has been the matter with him, and, in order to effectually hide it, carefully avoids doing the right things for fear that the world will suspect the truth

I believe that there should be no exceptions made in telling a person that he has the disease In one of my cases I refrained from telling the patient what was the matter with her because her family insisted and said that it would kill her, as just a year before, she had lost a favorite niece with laryngeal tuberculosis After a month's treatment, with very little improvement, I finally persuaded the family to let me tell her, and *explain to her the curability of the disease*, and I have never seen such a marvelous change She told me that she felt sure from the beginning as to what was the matter with her, and believed her case to be incurable since I was afraid to tell her Her knowledge as to the course of the disease was limited to the case of her niece, and she dreaded, night and day, the onset of the laryngeal symptoms, which she thought must come, and really feared this horrible torture more than she did death itself This patient has been an "arrested" case for five years, weighing more now than she ever did, living a normal life, and earning a salary (not "getting one") that many men would envy

To the second essential, going to a sanatorium or health resort, there are a number of exceptions, and it is at this point that you take up the all important factor, namely, the treatment of the individual and not the disease One of the greatest mistakes that we doctors make is to treat a disease, and not the patient who is suffering from it In no disease that I know of

is it so necessary to modify, or vary, your treatment according to the individual and his symptoms as it is in pulmonary tuberculosis

You must now consider what your patient is worth, how he earns his living, who are dependent on him, and how he will support himself should he be lucky enough to "arrest" his disease within a reasonable time Find out from him how long a time he can get from his firm or employer, whether his position will be given back to him when it becomes known that he has tuberculosis, and if the position is likely to be lost, how he can support himself, and those dependent on him, after his disease has become "arrested " To advise a man to go West who has no money, and who has far advanced tuberculosis or active symptoms, generally means not only a marked shortening of his life but also additional physical and mental suffering, to say nothing of the imposition put upon the charity of the community to which he goes It is most unfortunately true that, other things being equal, the man who has sufficient dollars has a far better chance of a long and useful life than one who has not, and that he who can earn the largest wage with the least expenditure of energy has the best chance

Some years ago a young schoolteacher consulted me She was exceptionally well educated in her profession, but absolutely dependent on it She had an incipient case of pulmonary tuberculosis with distinct but moderate symptoms To have her sent to Saranac, or Asheville, or Colorado would have prevented her from continuing her life's work, as no school board would have employed her, even though she had no cough and no sputum To have deprived her of her livelihood in order to check her symptoms would have been malpractice, and in her case I put her under a young doctor in the country who had been a patient and an intern at a well-known sanatorium After six months' treatment she took up her teaching duties, free of all symptoms, and feeling better than she had ever felt before, and, up to the time I last heard of her, had remained a "clinical cure," and, what is most important, I believe that she was less of a danger to the scholars than any other teacher in that institution

It is only by a careful study of the individual, not only from the medical standpoint but from every standpoint, that you are justified in allowing a patient with *active* symptoms to remain away from a sanatorium or resort. If the tuberculosis that you find through history, physical examination, or other means is not active, and is, perhaps, of long duration, resort or sanatorium treatment may not be necessary, but you have failed in your duty if you do not convince such a patient that he has a chronic disease, pulmonary tuberculosis, and thus give him the first essential in the cure

The choice of resort or sanatorium is again an individual requirement, and the only broad rule that I have used is to send my elderly patients to a Southern climate and my younger ones to the climate or section that they prefer

Another factor that is essential is to make your patient understand that it is not the climate or altitude that will cure him, but *the life he lives in that climate* I have never sent a patient to Saranac or Asheville, but have sent them to certain doctors in Saranac or Asheville who will treat them, educate them, and control them, so that when they leave the resort they can if they wish continue the cure, but, as Sir William Osler said, the cure of a patient depends much more on what he has in his head rather than what he has in his chest

The one fundamental truth in treating the active stage of the disease is "rest in proportion to the severity and duration of the symptoms "

CLINIC OF DR. PAUL W CLOUGH

FROM THE MEDICAL CLINIC OF THE JOHNS HOPKINS' HOSPITAL

PNEUMOCOCCUS SEPSIS

Sepsis in Contradistinction to Local or Focal Infections   Full Discussion of Symptoms, Prognosis, and Treatment.

THE patient whom we shall present to you illustrates some of the features of the most serious sequel of acute lobar pneumonia—a general pneumococcus sepsis

The patient is a colored man, twenty years of age, who was admitted to the Johns Hopkins Hospital eighteen days ago, complaining of pain in the stomach and side   His past history is unessential save that he has been a heavy smoker, and that in his occupation as driver he has been much exposed to inclement weather   The present illness began twelve days before admission, with pain in the left side of his chest, cough, and loss of appetite   These symptoms gradually increased in intensity, but did not force the patient to go to bed until five days later   In addition to the symptoms already mentioned, he then complained of very severe pain in the side, fever, marked shortness of breath, constipation, and vomiting, which persisted up to his admission

On admission he looked moderately ill, was mentally clear and alert. The respirations were accelerated, 40 to 60 per minute, with dilatation of the alæ nasi, and a well marked expiratory grunt. The temperature was 104° F, the pulse 120   There were typical signs of consolidation of the right upper and lower lobes, but not of the middle lobe   The left lung was clear

The heart was not enlarged   The relative dulness measured 10.5 cm to the left in the fifth space, and 4 cm to the right in

the fourth   The first sound was normal in character, and was followed by a soft systolic blow, which was not transmitted to the axilla

The examination of the blood showed   R B C , 6,000,000, W B C , 11,500, Hb , 90 per cent   A blood-culture yielded no growth

The sputum was mucopurulent and streaked with blood. On culture, a pneumococcus belonging to Group IV was isolated

Urine   Orange, acid, 1022 sp gr , trace of albumin, a few hyaline and granular casts   The chlorids were suppressed

The clinical diagnosis was acute lobar pneumonia due to the pneumococcus, with consolidation of the right upper and lower lobes

The temperature fell by lysis on the eleventh and twelfth days, reaching normal on one observation   The general condition seemed improved, but no definite change in the physical signs in the chest could be made out   On the thirteenth day, however, the temperature rose to 101° F , and continued to rise, till on the sixteenth day it reached 104 5° F   From this time up to the present there has been a persistent, irregularly remittent fever, ranging from 101° to 106° F , which figure has been reached several times   There has been an increasing tachycardia, roughly proportional to the height of the fever, and also moderate tachypnea

With the recrudescence of fever the various causes for persistent fever were successively considered   Let us enumerate the more important ones   (1) Empyema   (2) Delayed resolution, including abscess formation   (3) Pneumococcus sepsis (4) Extension of the pneumonic process to a previously uninvolved lobe   (5) Otitis media   (6) Pericarditis   (7) Pulmonary tuberculosis   (8) Serum disease   (9) Accidental or coincidental infections, not a direct sequel of the pneumonia

In the discussion of these complications it will be convenient to consider, first, those which could most easily be ruled out, and take up later those which had to be considered most seriously in this patient

Extension of the consolidation to other portions of the lung could be ruled out by physical examination   Otitis media was sim-

ilarly excluded No evidence was obtained suggesting the existence of any accidental or intercurrent infection Pericarditis was watched for, but no pericardial friction rub was heard, and, in particular, there was no evidence of a developing pericardial effusion While much less common than empyema, a pericarditis with a purulent effusion is an occasional complication of pneumonia, and a fatal one if it is not recognized and submitted to surgical treatment.

Pulmonary tuberculosis was also considered Lobar pneumonia may, of course, occur in an individual with active pulmonary tuberculosis, or a latent tuberculous lesion may be aroused to activity by an attack of pneumonia In either case persistent fever due to the tuberculosis may continue after the high fever of the pneumococcus infection has subsided In some cases, too, as has been emphasized by Dr Osler, an acute pneumonia, for a time clinically indistinguishable from a pneumococcus lobar pneumonia, may be caused by the tubercle bacillus, a true acute tuberculous pneumonia, and be recognized only on finding tubercle bacilli in the sputum In this case repeated examinations of the sputum for tubercle bacilli were made, all with negative results There was no evidence of tuberculosis in the left lung or elsewhere in the body

Serum disease did not enter into consideration in this patient, since he received no serum The only serum therapeutically effective is that active on pneumococci of Type I, and the pneumococcus infecting this patient belonged to one of the other types Patients with Type I infection who have repeatedly received large doses of serum, quite independently of the occurrence of immediate reactions of an anaphylactic type, not infrequently show late elevations of temperature These, when they occur, usually come on ten or twelve days after serum is first administered, the temperature frequently reaches 102° to 103° F, and the fever usually persists for about a week, often in association with urticarial eruptions, joint pains, and a moderate degree of prostration In exceptional cases, however, a more severe type occurs [1] The fever may persist for two, three,

[1] Bloomfield, A. The Effects of Serum Therapy in Acute Lobar Pneumonia Johns Hopkins Hosp Bull, Baltimore, 1917, xxviii 301–306.

or even five weeks It may be high, with irregular remissions. There is usually marked general malaise and prostration, severe aching pains and stiffness of the joints and of the body generally, and often recurring attacks of urticaria There may be a marked general glandular enlargement, albuminuria and cylindruria, and a high leukocytosis, even as high as 20,000 to 40,000, with (inconstantly) an eosinophilia Fortunately, such severe re actions are rare, and, as far as reported, complete recovery has always occurred They may cause serious diagnostic difficulties to those unfamiliar with them

In this patient empyema was at first regarded as the most probable explanation of his fever, and, as should be done with every patient with pneumonia, the chest was examined daily with special care to detect any signs indicating an accumulation of fluid No such signs could be made out There was no significant change in the leukocyte count, which varied from 7500 to 12,000 Had there been anything found on physical examination to suggest fluid, an x-ray examination of the chest would have been made, and if doubt still existed, an exploratory puncture over the most suspicious area with a small aspirating needle An x-ray examination should have been made, notwithstanding the absence of suggestive physical signs, since not infrequently the x-ray plate may furnish the first definite evidence of fluid, particularly if it is encapsulated between the lobes Furthermore, in any case where there is a suspicion that an empyema may be developing, it is desirable to have plates taken at frequent intervals for purposes of comparison These considerations usually outweigh the slight discomfort to the patient involved in such an examination, at least in a well-arranged hospital where the x-ray room is in close proximity to the ward

Delayed resolution of the consolidated lung tissue may be associated with long-continued fever This may last a few weeks, or even for two or three months, eventually to subside completely, with apparently absolute restoration of the lung tissue to normal Or in some cases partial organization of the exudate occurs, and a chronic fibroid pneumonia ensues, often associated with multiple small abscesses, which, as a rule, runs a protracted

course, often to end in death The diagnosis of delayed resolution may be made as an explanation for persistent fever only after all other possible causes for fever have been excluded

Finally, we had to consider the possibility of an invasion of the blood stream by the pneumococcus, a generalized pneumococcus sepsis As a cause of such a recrudescence of fever as occurred in this patient this is fortunately less frequent than is empyema or simple delayed resolution It is not of rare occurrence, however, and its existence must be suspected in every such case The diagnosis may sometimes be reached by the demonstration of those secondary or metastatic foci of infection which we know to be most frequent in pneumococcus sepsis, particularly purulent arthritis, acute endocarditis, and purulent meningitis. It is established with certainty by the cultivation of pneumococci in considerable numbers from the blood stream

To return to our consideration of this patient, on the eighteenth day of the disease, and the fifth day of the recrudescence of fever, he showed slight jaundice, a symptom which is not infrequent among our colored patients, and which is not necessarily of bad prognostic significance He was mentally clear and seemed, on the whole, in better general condition than on admission Respirations were moderately accelerated, but not labored Signs of consolidation persisted over the right upper lobe and upper part of the lower lobe, but the right base was resolving The left lung was still clear

The heart showed no change The apex was inside the mammillary line, and the sounds normal except for the soft systolic blow noted on admission The leukocyte count was 7500 A blood-culture was made, from which a day or two later the pneumococcus was isolated Unfortunately, there is no note in the report of this culture as to the number of colonies developing per cubic centimeter of blood However, any appearance of organisms in the blood at this stage of the disease, in association with fever of this type which is otherwise unexplained, is strong evidence of the development of sepsis

Four days later, on the ninth day of the recrudescence, clinical evidence of sepsis was made out The heart was found

to be dilated   The dulness measured 12 cm to the left and 5 cm to the right of the midline   The first sound at the apex was loud and thudding and was followed by an intense systolic blow, well transmitted to the axilla   The pulmonic second sound was definitely accentuated   Along the left sternal border, and maximal in the third left interspace, there was a short diastolic puff   The change in character of the systolic murmur, and especially the appearance under observation of the diastolic murmur, in association with the fever, and the presence of organisms in the circulating blood, indicated definitely the development of an acute pneumococcus endocarditis, involving, in all probability, both the mitral and aortic valves   There was no significant change in the lungs   Blood examination revealed the development of a secondary anemia   The red blood-cells had fallen to 4,000,000 and the hemoglobin to 60 per cent. The development of a secondary anemia is usually a striking feature in all forms of sepsis

A second blood-culture corroborated the results of the first one and showed the presence of large numbers of pneumococci

The patient today is in the twenty-sixth day of the disease   His general condition is very much worse   The temperature is elevated (105°F), the pulse rapid, 120 to 130, respiration 32, moderately accelerated   The leukocyte count has risen to 17,000   The lungs show no change, except that in the left interscapular region there is an area of dulness and enfeebled breath sounds, indicating probably a beginning consolidation on that side   The heart shows the same findings as on the previous examination, although the restlessness of the patient makes auscultation very difficult   A very marked change in the mental state has occurred during the past twenty-four hours   He is now quite irrational and confused   He does not know where he is, and does not recognize those about him   He is restless, and has several times attempted to get out of bed   He does not carry out commands or co-operate at all in the examination   He lies with his head and eyes deviated to the right   The pupils are equal and react to light   There is slight strabismus, the right eye tending to turn outward   Ophthalmoscopic examination

has shown nothing abnormal except slight engorgement of the veins

His neck is very stiff, and attempts to flex it result in lifting the shoulders of the patient off the bed There is a coarse tremor of the arms The limbs are rigid, and any attempt at passive movement meets with resistance The knee-jerks are exaggerated and there is an ankle-clonus on both sides, more marked on the left than on the right. Plantar stimulation gives an equivocal response There is a well marked Kernig sign.

On the basis of these findings a definite diagnosis of menin gitis was made, and has been confirmed by lumbar puncture The spinal fluid was turbid, and microscopically showed large numbers of pus-cells and Gram positive lance-shaped diplococci

To summarize This patient on admission presented the picture of an ordinary acute lobar pneumonia, with consolidation of the right upper and lower lobes A Group IV pneumococcus was isolated from the sputum. After a transient remission in fever and symptoms on the eleventh and twelfth days, there was a recrudescence of fever, with the development of a general sepsis, as shown by the appearance of large numbers of pneumococci in the circulating blood, and the development of acute endocarditis and purulent meningitis.

By sepsis we understand a more or less generalized invasion of the tissues and fluids of the body by micro-organisms, in contradistinction to local or focal infections, in which the organisms remain localized in a single region In order that sepsis may develop it is essential that micro-organisms invade the tissues of the body, and give rise somewhere to an infection which at first is more or less definitely localized The mere accidental penetration of a few organisms into the blood never directly gives rise to sepsis, at least in human infections The organisms, under conditions unfavorable to the host, may multiply in this primary focus of infection, penetrate from it into the blood or lymph stream, and be transported to all parts of the body The most important mechanism for their dissemination is probably the formation of infected thrombi in the small veins of the inflamed area From these infected thrombi minute emboli con-

taining bacteria may be continually broken off and carried away in the blood-stream   We then have a septicemia   The organisms which have gained entrance into the blood speedily lodge in the capillaries of the various organs, where, as a rule, they are destroyed without harm resulting   If, however, the organisms happen to lodge in some spot where the local conditions are especially favorable for their growth, they may multiply, and give rise to secondary, or metastatic foci of infection. If multiple abscesses develop in the viscera as a result of such a dissemination of pyogenic cocci, the condition is termed "pyemia "

Whether an infection shall remain localized or whether there shall be an invasion of the blood-stream and a general dissemination of the infection depends on the balance between the virulence, or invasive power of the micro-organisms, and the defensive powers of the host   The mechanism of these reactions is extremely complicated, and differs, in details at least, in case of infections with different species of micro-organisms   Despite the large amount of study devoted to it, our knowledge of the subject is still very meagre, especially as to the part played by the bacteria   In the defensive reaction of the host, simple mechanical factors play a rôle, such as the vascularity of the infected tissue, and the barrier to the spread of infection by continuity which may be interposed by dense connective-tissue capsules, fasciæ, or muscle sheaths   There are also concerned active functions of the tissue cells, and of the phagocytes, and various antibacterial, and possibly antitoxic properties of the blood plasma   The protective properties of the blood-serum are somewhat more thoroughly understood, and in a few instances they may be effectively supplemented by therapeutic administration of immune serum

By a combination of those factors the body in most instances successfully combats the spread of an infection   Even the entrance of a few organisms into the blood-stream is ordinarily without significance   In the blood the organisms, as a rule, find conditions unfavorable for their growth and multiplication   The blood-stream serves only as a means of transporta-

tion, not as a culture medium The continued presence of
organisms in the blood means, therefore, a continuous dissem-
ination from some focal infection. If this focus can be removed,
the blood speedily becomes sterile It is only when the organisms
are repeatedly entering the blood stream in relatively large
numbers, and over a considerable period of time, that sepsis
with its attendant metastatic infections develops

In occasional cases, indeed, shortly before death there may
be such a tremendous increase in the number of organisms in
the blood that it seems probable that actual multiplication in
the blood stream has occurred This, however, is exceptional,
and probably indicates a final and complete breakdown of the
defensive forces of the body

The mere presence of a few organisms in the blood occasion-
ally, or even over considerable periods of time, does not con-
stitute sepsis. The latter exists only when organisms are present,
usually in considerable numbers, and when their presence is
associated with or portends the development of secondary
foci of infection. In many infections, essentially localized a
few bacteria occasionally penetrate into the blood, and may be
discoverable on culture, without their presence in the blood
having any evident significance To this condition the term
"bacteremia" is given The distinction is to some extent an
arbitrary one, and it may be a difficult one to make in an indi-
vidual case

micro-organisms cause no lesion at the point of entrance which is noticed by the patient, or which leaves any evidence of its existence   Without denying the possible existence of a minute local infection, the fact is certain that it may be insignificant and transient   Nevertheless, organisms may gain entrance to the blood, may be carried to some tissue in which conditions are favorable for their development, and may give rise there to a local infection which, to all intents and purposes, is primary, and from which a general sepsis with multiple secondary foci of infection may arise   A good example, in the case of Staphylococcus aureus infections, is the (so-called) primary osteomyelitis. While, strictly speaking, a primary osteomyelitis is impossible, the primary superficial infection is only a portal of entry, it is of significance only in opening a pathway for the invading micro-organisms to the susceptible focus in the bone

With these general principles in mind, let us consider the facts, so far as known, in regard to pneumococcus sepsis, and, in particular, to its most frequent form, that following acute lobar pneumonia   First let us review what is known concerning the presence of the pneumococcus in the circulating blood   It has been known for many years that pneumococci may be present in the circulating blood in pneumonia, but there has been the greatest diversity of opinion as to the frequency and significance of their presence   Some observers found positive blood-cultures in a majority of the cases, from 60 to 90 per cent , or even higher, and attached no special prognostic significance to their presence   Others obtained positive results in only 30 to 40 per cent of their cases, almost exclusively in patients who died of the pneumonia, and they regarded a positive culture as a sign of very ill omen

These divergent results as regards the demonstration of the organisms were probably due, in part, to actual differences in the frequency of blood invasion in different epidemics and in different localities, and, in part, to differences in technic   By the withdrawal of relatively large amounts of blood, at least 20 c c., by making daily cultures from the very onset to the termination of the disease, and by the use of media offering optimum

conditions for growth, a considerable number of positive cultures may be obtained, which would be missed if only a single routine culture were taken.

Jochmann,[1] who at first found organisms in only about 30 to 40 per cent of his cases, and rarely except in fatal ones, later, by the use of more refined methods of cultivation, and especially by the use of fluid media, obtained positive results in about 75 per cent. of his cases, and regarded a bacteriemia as one of the usual manifestations of the disease

The difference in the interpretation of the results was also due to the failure at first to recognize the importance of an ac curate quantitative determination of the number of organisms present per cubic centimeter of blood

It is now known that in a large majority of the patients who die of pneumonia, if repeated cultures are taken up to death, positive blood-cultures can be obtained. In general, the number of organisms per cubic centimeter of blood increases as death approaches, and cultures taken shortly before death usually show a considerable number

frequently, perhaps usually, a few organisms may occasionally invade the blood-stream, and that their presence does not unfavorably influence the prognosis   If the number exceeds 5 per cubic centimeter of blood, the outlook is less favorable If they exceed 15 to 20 per cubic centimeter, the outlook is very grave, unless it be in Type I infections, where some help may be hoped for from serum treatment   If large numbers are present, over 100 per cubic centimeter, the outlook is hopeless, an actual sepsis exists

In the study of pneumococcus sepsis it is desirable to consider pneumonia as one manifestation of an acute pneumococcus infection rather than as primarily a disease of the lungs The portal of entry of the infection is undoubtedly the mucous membrane of the respiratory tract   Recent investigations at the Rockefeller Hospital have shown that in a majority of the cases of lobar pneumonia the infection is acquired from an outside source, though it may be caused by a pneumococcus which has been a previously harmless inhabitant of the mouth or throat The weight of evidence at present seems to indicate that the pneumococcus usually reaches the lung by direct passage down ward through the bronchi, though the possibility of its reaching the lung by the blood or lymphatics is not entirely excluded Here it causes a localized infection which we may regard as the primary focus of infection   From an uncomplicated pneumonic consolidation a blood invasion may arise, and this is doubtless the source in most instances where the invasion occurs at the height of the disease   In cases where sepsis develops after an apparent crisis or lysis, it seems probable that some local complication is to be looked for as the site from which dissemination of organisms has occurred   Those most frequently found are areas of delayed resolution, especially if associated with abscess formation, empyema, or pericarditis

Pneumococcus sepsis may follow a bronchopneumonia due to the pneumococcus   This has been especially frequent in the secondary bronchopneumonias following measles and epidemic influenza, but it occurs less commonly than in ordinary lobar pneumonia

Pneumococcus sepsis may also arise from primary foci of infection in the upper respiratory tract. Most important are acute tonsillitis, acute paranasal sinusitis, and especially otitis media, and its sequelæ, acute mastoiditis, sinus thrombosis, and meningitis. Pneumonia occasionally develops as a metastatic infection, in sepsis arising from one of these latter sources.

Other sources of origin of a pneumococcus sepsis are on record, but are of interest chiefly because of their rarity. They need not be considered here.

Why secondary foci of infection develop in some patients with sepsis and not in others is not known. The duration of life after the onset of the blood invasion is certainly an important factor. The longer the patient lives, the more likely it is that such infections will develop. That they may develop with great rapidity, however, is shown by a brief reference to another case history. This patient entered with a lobar pneumonia which terminated by crisis on the fifth day. After two days of continuously normal temperature there was a sudden recrudescence of high fever, and on the second day of this recrudescence clinical signs of aortic and mitral endocarditis appeared.

The clinical symptoms of sepsis depend on the stage of the disease in which the blood invasion occurs, on the rapidity of its course, and on the presence of the various secondary localizations of the infection, and their prominence.

Most often, probably, the blood invasion occurs at the height of the disease, and leads speedily, as a rule, to a fatal termination, without any remission either in the symptoms or the fever. There are often no specific symptoms pointing to the blood invasion, and the diagnosis can be made only by blood-culture. Suspicion may be aroused by rapid deterioration in the patient's general condition, or by evidences of increasing intoxication. There may be some rise in the height of the fever, progressive tachycardia, increasing cyanosis, often tympanites, tremor, delirium, or at times coma, though many patients remain mentally clear throughout the course. Such patients at autopsy often show no evidence of local infection outside the lungs and pleura, and occasionally the pericardium. In other

cases, especially if death does not occur promptly, metastatic areas of infection may develop, though they are often overlooked clinically

In other patients, such as the case just presented, there may be a remission in both the fever and the subjective symptoms The respirations become slower, the dyspnea and cough less distressing, the prostration and general discomfort less marked Sometimes two or three days of completely normal temperature may intervene, though, in our experience, this is unusual. Then there is a rise in temperature for which, at first, there is no obvious explanation, and an increase in the pulse and respiration rate, usually moderate at first, and usually without the pain and dyspnea that prevailed during the primary pneumonia. There is usually headache, prostration, and general malaise proportional to the height of the fever, but for a time these general symptoms may be surprisingly slight, and the mental state quite clear and alert   There is frequently clinical evidence of delayed resolution, and nothing else of significance on physical examination   As a rule, the diagnosis is possible at this stage only by means of a blood-culture   If this method of diagnosis is neglected, the condition will often be overlooked, and can be recognized only by demonstrating the existence of metastatic infections   In the case of pneumococcus sepsis, as already stated, the tissues most frequently involved are the joints, the heart valves, and the meninges

Acute arthritis is very important clinically, because it is rarely overlooked   It occurred in Musser and Norris'[1] collected statistics in about $\frac{1}{2}$ per cent of all cases of pneumonia   There is a relatively benign type of arthritis attended by mild local symptoms, with a serous and usually sterile effusion, which generally subsides under symptomatic treatment, and is not associated with sepsis   More frequent and much more important is an acute purulent arthritis   This form is often mono-articular, though it may be polyarticular   It is apt to attack the larger joints, most often the shoulder, or knee, in the cases I

[1] Musser, J H, and Norris, G W   Lobar Pneumonia, in Mod Med (Osler), 1907, ii, 537–646

have seen The joints are very painful and tender, much swollen, and reddened On aspiration, purulent fluid containing large numbers of pneumococci is obtained This form is of the gravest significance because it is usually one manifestation of a general sepsis, which is practically always fatal Occasionally, however, a purulent arthritis may be independent of a general sepsis, or be the only secondary localization, and under such circumstances recovery is possible. Some permanent damage to the joint usually results unless suitable surgical treatment is employed

Acute endocarditis is the most frequent and most important of the secondary infections in pneumococcus sepsis In Musser and Norris' statistics it was recognized clinically in about ½ per cent of all cases of pneumonia In their autopsy statistics, however, it was present in over 5 per cent of the cases This discrepancy indicates that the diagnosis is made in only about one-half the cases in which endocarditis occurs

Acute endocarditis is always a part of a general sepsis Subjective symptoms referable directly to the endocarditis apart from those of sepsis are usually slight or absent. The diagnosis depends on the objective findings of a thorough physical examination of the heart. There is no type of fever that is at all constant or characteristic The temperature is most frequently high, with irregular remissions, but it may be maintained at a surprisingly constant level In some cases intermittent fever occurs, and with this type there may be chills and sweats, but aside from a chill at the outset of the sepsis, which is not uncommon, these symptoms are exceptional Afebrile periods, or periods of slight fever, characteristic of the subacute form of bacterial endocarditis due to Streptococcus viridans, are very rare

There may be unusually marked tachycardia. There is usually demonstrable a progressive dilatation of the heart, and changes in the character of the sounds, as well as the appearance of murmurs, which indicate the development of valvular defects. Diastolic murmurs, when present, are more significant than systolic murmurs. A soft systolic blow, especially if un

associated with changes in the first sound at the apex, and best heard over the right ventricle, means very little   If, however, the murmur is intense, if the first sound is sharp, or is muffled or obliterated, if the murmur is well transmitted to the axilla, and the pulmonic second sound is accentuated, the probability of valvular disease is very much greater   On the contrary, there is little room for doubt as to the significance of a diastolic blow, since this is rarely the result merely of muscular relaxation The development under observation of such endocardial mur murs, in association with the presence of many pneumococci in the circulating blood, makes the diagnosis reasonably certain Practically all doubt is removed if embolic phenomena occur These, however, are often absent, especially in those cases which run a rapid course

The following case history illustrates some of the more com mon types of embolism in acute pneumococcus endocarditis

This patient, a colored man twenty years of age, was admitted to the ward on the fifth day of an acute lobar pneumonia   He had had a typical attack of acute rheumatic fever three years before, and had been told that his heart was affected by it. Physical examination on admission showed signs of consolidation of the left upper and lower lobes   The heart was moderately enlarged, the apex impulse in the fifth space, 12 cm from the midline   There were signs of mitral and aortic in sufficiency   Temperature 104° F   Pulse 120   Respiration 48 W B C 18,000   The pneumococcus was cultivated from the sputum   Blood-culture gave no growth   On the ninth and tenth days there was a remission in the fever, which varied from 99° to 101° F , and a corresponding improvement in his general condition   The pulse fell to 70–80, the respirations to 24, the W B C to 8000   The temperature did not reach normal, but during the next week fluctuated between 99° and 101 5° F   Nothing was found on physical examination to explain the fever   In particular, there was no evidence of empyema The physical signs in the lungs indicated a progressive resolution of the consolidated areas, at about the average rate

On the eighth day after the remission (eighteenth day of the

disease) the temperature rose to 104° F Pulse 90 Respiration 24–32 W B C 7400 The patient was alert, complained of headache and of feeling tired, was dyspneic on very slight exertion The lungs had almost cleared The heart was more enlarged, the dulness measured 15 cm to left and 5.5 cm. to the right. The first sound had disappeared, the systolic murmur was more intense, and was now audible in the back. The pulse was more collapsing, and there was an extraordinary degree of throbbing in the peripheral vessels It was thought that an acute endocarditis had been superimposed on the pre-existing chronic rheumatic endocarditis A blood-culture revealed the pneumococcus At that time the importance of determining the number of organisms present was not appreciated

The patient lived just four weeks, and during this time had a high remittent fever, varying from 100° to 105° F. Embolic phenomena occurred as follows On the twelfth day of the recrudescence there was pain in the chest, dyspnea, cough, and tenacious sputum mixed with bright red blood, suggesting a pulmonary infarction

On the thirty-third day there was a cerebral embolism, with left hemiplegia

Death occurred on the thirty-seventh day Autopsy report Acute vegetative and chronic endocarditis of mitral, aortic, and tricuspid valves, infarcts in the myocardium, brain, and spleen, abscesses in the kidneys, acute fibrinous pleurisy; chronic adhesive pericarditis

While a pre-existing chronic valvular lesion doubtless predisposes to the implantation of an acute pneumococcus infection on the valves, as in this case, it is by no means essential In many cases previously normal valves are attacked The mitral valve is most frequently affected, the aortic somewhat less frequently The valves on the right side are less often involved, but the preponderance of left-sided lesions is somewhat less marked than in rheumatic endocarditis Anatomically the diseased valves show vegetations which may become very large and polypoid, and ulceration and rupture of the valve frequently occurs The course is usually acute, the disease lasting from a few days to a few weeks, and the outcome is practically always fatal It is doubtful if protracted cases, lasting for months, are ever due to the pneumococcus Such cases reported in the earlier literature were probably due to Streptococcus viridans.

The third important metastatic infection in pneumococcus sepsis is meningitis As a sequel to pneumonia it rarely occurs except in association with sepsis In sepsis, either endocarditis or meningitis may occur without the other, but they are associated in about half of the cases in which they occur It is slightly less frequent than endocarditis, being recognized clinically in 0 4 per cent. of Musser and Norris' series, but was found at autopsy in $3\frac{1}{2}$ per cent of their cases Like endocarditis, therefore, it is recognized clinically in only about one-half of the cases in which it occurs

Its recognition is simple in cases, such as the one presented, where typical symptoms are present As in this case, the onset of this complication is frequently suggested by a marked change in the mental state There is often, at first, irritability, restlessness, and delirium, associated with a general hyperesthesia

Later the condition changes to apathy, stupor, or profound coma, or the condition may be characterised from the start by a gradually increasing stupor There may be tremor or muscular twitchings, with spasticity of the limbs and exaggerated reflexes Highly characteristic, when they occur, are paralysis of one or more cranial nerves, most frequently the third or sixth, with a resulting strabismus, marked stiffness of the neck, and a positive Kernig's sign It is important to remember that these symptoms and signs are often absent, that meningitis will often be unsuspected unless the patient is very carefully watched, and that a definite diagnosis can often be made only by examination of the spinal fluid The difficulty in diagnosis is further increased by the well known fact that in pneumonia, as in many acute infectious diseases, the clinical symptoms and signs of meningitis may be present in marked degree, and yet lumbar puncture reveals a normal spinal fluid, and the patient recovers A state of meningeal irritation, or meningismus, exists, which must be attributed to the local action of some toxin, and is not dependent on the actual presence of organisms in the meninges

Recently a word of warning has been raised as to a possible danger from indiscriminate lumbar puncture The work of Austrian,[1] with the meningococcus in rabbits, and of Weed[2] and his associates, with the Friedländer bacillus in cats, and the streptococcus in rabbits, has shown that if a septicemia is produced, such simple procedures as the injection of a small amount of normal serum into the subdural space, or merely the removal of spinal fluid, may precipitate an infection of the meninges by the organisms in the blood-stream

There is at least a theoretic possibility that a similar infection of the meninges from the blood might be precipitated in patients by lumbar puncture Indeed, we have seen one case of typhoid fever in which a typhoid meningitis developed three

[1] Austrian C. R. Experimental Meningococcus Meningitis Johns Hopkins Hosp. Bull., Baltimore, 1918 xxix, 183–185

[2] Weed, L. H Wegeforth P., Ayer J B and Felton L. D The Production of Meningitis by Release of Cerebrospinal Fluid During experimental Septicemia Jour Amer Med Assoc., Chicago 1919 lxxii, 190

days after an exploratory lumbar puncture, by which a normal fluid, sterile on culture, had been obtained It would seem safer, therefore, to be conservative in the employment of this procedure, especially if organisms are present in the blood, except in the case of Type I infections, where the demonstration of a meningitis would be an indication for the subdural injection of immune serum

The outlook in pneumococcus meningitis is extremely bad, though a few authentic cases of spontaneous recovery are on record It is hopeless if the meningitis is a manifestation of a general sepsis The study of experimental pneumococcus infection has shown that in the dog,[1] an animal which has a high natural resistance to pneumococcus infection, or in the rabbit,[2] if treated with injections of immune serum, an intravenous injection of pneumococci may be followed by disappearance of the organisms from the circulation, and yet death may occur later from meningitis, although the blood remains sterile. During the brief period of artificially produced septicemia organisms penetrated into the subdural space, where they were able to multiply and give rise to a fatal infection, probably because there they are not exposed to the antibacterial activities of the blood It seems probable that an analogous condition may occasionally develop in man, and it would be in these cases especially that help might be expected from the intraspinous injection of immune serum in Type I infections The same would be true in the occasional cases of so-called primary or cryptogenic pneumococcus meningitis which develop independently of pneumonia

Other localizations of infection in pneumococcus sepsis are less frequent and less important Among those described may be mentioned otitis media, peritonitis, acute thyroiditis, thrombophlebitis, and muscular abscesses It is remarkable that the pneumococcus rarely gives rise to some of the lesions so often

---

[1] Bull, C G Immunity Factors in Pneumococcus Infection in the Dog, Jour Exper Med , Baltimore, 1916, xxiv, 7

[2] Bull, C G The Mechanism of the Curative Action of Antipneumococcus Serum, Jour Exper Med , Baltimore, 1915, xxii, 457

found in sepsis due to the pyogenic cocci, especially to osteo-myelitis and to abscesses of the skin, kidneys, and myocardium

It is frequent to find an acute fibrinous pleurisy, an empyema, or a pericarditis in patients with sepsis. Indeed, an empyema or a pericarditis may be the starting point of a sepsis, but these lesions frequently and, indeed, usually develop and run their course independently of sepsis

TREATMENT

The prognosis after sepsis is established is practically hopeless, and all forms of treatment have been futile. Even when no evidence of metastatic infection can be made out, if extensive invasion of the blood-stream has occurred, recovery is excessively rare. We must try by preventive measures to lessen the possibility of the development of sepsis. We need not discuss here the ordinary symptomatic and supportive treatment of pneumonia. The question uppermost in the mind of everyone must be, Have the recent advances in the methods of preparing and standardizing immune serum, and especially in determining the most effective mode of administration made the serum so effective therapeutically that it ought to be used as a routine method of treatment?

The answer to this question must be sought in the published reports of those who have had the largest experience in its use. The favorable reports in Type I infections published by Cole[1] and his associates at the Rockefeller Hospital, supported by those of medical officers from several of the army camps, are convincing, and seem to have established the value of the treatment in these cases. While we are not in a position to make an authoritative statement on the basis of our own limited experience, I feel that we must agree with the recent statement of Nichols[2] that "This method of treatment has passed the experimental stage, and no patient with Type I infection who

[1] Cole R. I. Treatment of Lobar Pneumonia, Med. Clinics of North America 1917 i 545

[2] Nichols, H. J. The Lobar Pneumonia Problem in the Army New York Med. Jour., etc., 1917, cvi 219-223

dies without the early intravenous administration of large doses of Type I serum can be said to have received the best treatment."

If serum treatment is to be beneficial it must be properly carried out   No physician should attempt to administer it until thoroughly familiar with the principles underlying the treatment, with its limitations and possible dangers, and with every detail in its performance   The essential points have been simply and comprehensively discussed in Monograph No 7 of the Rockefeller Institute,[1] which should be carefully studied by every one who intends to administer serum

I should like to refer very briefly to a few of the more important considerations   As is now known, pneumococci belonging to different types behave, in their reactions to immune serum, as distinct species of micro-organisms   A Type I serum which is highly effective against Type I organisms has no appreciable activity toward pneumococci of Types II, III, or IV While immune serum of considerable potency has been prepared for Type II pneumococci, this serum is considerably less effective in protecting animals from infection with Type II organisms than is Type I serum with Type I pneumococci   Furthermore, Cole has concluded that in the treatment of Type II pneumonia in man this serum has little, if any, therapeutic value   The immune serum thus far prepared with Type III organisms has shown such feeble activity in animal experiments that its use in human infections has been deemed unjustifiable   If it were possible to prepare effective immune sera with Type II and Type III pneumococci, a practicable method could probably be devised for immunizing an animal simultaneously to organisms of each of these three types   With such a polyvalent serum, one might feel justified in treating patients with pneumonia without regard to the type of the infecting organism in each individual case, knowing that in 75 to 80 per cent of the patients, on the average, the infecting organism would be susceptible to the activity of such a serum   However,

[1] Avery, O , Chickering, H T , Cole, R., and Dochez, A. R   Acute Lobar Pneumonia, Prevention and Serum Treatment, New York, 1917, Rockefeller Institute for Medical Research

until an effective serum can be prepared for pneumococci of Types II and III the use of polyvalent serum in infections with these types is futile and deceptive, and as a routine measure, at least, the use of serum should at present be restricted to patients with Type I infection Fortunately, this type is the one most frequently met with in pneumonia in this country, being found in 30 to 40 per cent of the cases, and it is one which causes a high mortality if serum treatment is not employed

For these reasons the determination of the type of pneumococcus concerned in each case should be an indispensable pre requisite to serum treatment, except perhaps in emergencies The time and labor involved in the type determination is not an adequate excuse for the omission of this procedure The neglect of this precaution means that one needlessly subjects those patients who are infected with pneumococci of Types II, III, and IV, and who makes up about 60 per cent of all cases of pneumonia, to the discomfort of the injections and to the possible danger of serum reactions

If one is dealing with a Type I infection, the treatment should be begun as early in the disease as possible, and should be carried out, as prescribed, by the repeated intravenous injections of large doses of serum until the temperature falls and the general condition is improved Little can be expected from the use of serum if inadequately administered, or if it is used only as a last resort in patients who have become desperately ill

CLINIC OF DR. ARTHUR L BLOOMFIELD

JOHNS HOPKINS HOSPITAL

THE CLINICAL DIAGNOSIS OF EPIDEMIC INFLUENZA[*]

INTENSIVE bacteriologic and epidemiologic study of the recent epidemic has failed as yet to establish the etiologic agent On the clinical side, as well, there exists much uncertainty and confusion as to the identity and diagnosis of the disease The descriptions of influenza, both as seen in military camps and in civil life, have been meager and inadequate, appearing usually as brief notes preliminary to bacteriologic reports. While nearly all observers agree that the disease begins as a local inflammation in the respiratory tract, there is sharp difference of opinion as to whether the bronchopneumonias are secondary and in the nature of a complication, or whether they are a primary and essential feature Thus Hewlett,[1] Keegan,[1] Nuzum,[3] Fantus,[4] Soper,[5] and Hall[6] regard pulmonary involvement as a complication or sequel to a primary disease which itself is of uncertain nature Christian,[7] on the other hand, regards influenza as "a disease involving the respiratory tract", and Strouse[8] speaks of it as "the epidemic of respiratory disease," since he finds in a large percentage of cases at onset pulmonary signs suggestive of bronchopneumonia. Hirsh[9] refers to the "epidemic of bronchopneumonia", Friedländer[10] distinguishes types of the disease featured by either coryza, bronchitis, pneumonia, or acute pulmonary edema, Blanton[11] differentiates prepneumonic and pneumonic stages, Synott[12] regards it as primarily an upper respiratory tract infection, and Ely[13] assumes pulmonary involvement from the start. The special committee of the American Public Health Association states in its report[14] that there

is no known method by which an attack of influenza can be differentiated from an ordinary cold or bronchitis

A scrutiny of these reports shows that confusion as to the nature of the clinical picture has arisen in two ways in the first place, by regarding the pneumonias which complicate or follow epidemic influenza as the primary disease, and second, by mistaking for influenza localized respiratory tract infections which are not influenza at all It seems of the greatest importance to establish, if possible, criteria by which one can distinguish definitely between true cases of epidemic influenza and other diseases Until this is done etiologic and epidemiologic studies will be greatly hampered In a previous paper[15] it was pointed out that the disease at the height of the epidemic presented a distinct clinical picture which could be recognized apart from pulmonary complications, a constant set of symptoms, characteristic erythema of skin and mucous membranes, fever of determinate duration, and leukopenia were the main features It was also noted that as soon as the peak of the epidemic was passed a remarkable change took place in the type of the disease, the symptoms were much less severe, the hyperemic phenomena were much less marked, and the incidence of pneumonia decreased It is the present purpose to point out that while the disease, as seen since the great wave of the epidemic passed, is less picturesque than the fulminating type, it none the less preserves definite clinical features which make it recognizable and distinguishable from non-influenzal respiratory infections

Seventy-eight consecutive cases admitted to the Johns Hopkins Hospital during November, December, and January form the basis of this report Since the clinical picture was systematically described in the previous paper, only those points in which the postepidemic* disease differs from the epidemic form or which are of importance in the differential diagnosis will be considered

Symptoms —No essential difference of symptoms was seen

* "Postepidemic" is used in this paper to designate the cases of influenza which have occurred since the sudden wave of the disease in October, 1918

in the epidemic and postepidemic cases, save that the latter were, as a rule, less severe   Headache, pain in the eyes, general aching, malaise, anorexia, and nausea were the usual complaints   The absence of local symptoms referable to the respiratory tract was even more striking than at the height of the epidemic   If present at all, there was simply slight rawness of the throat, with dry, unproductive cough, stoppage of the nose with a little watery secretion, and conjunctivitis   There was no sharply localized lesion, but the condition was one of diffuse hyperemia of the air passages, somewhat similar to that seen after the application of a chemical irritant, such as adrenalin   Unless a local complication supervened the hyperemia and its accompanying symptoms usually subsided within two or three days   The tremendous prostration seen during the epidemic did not occur in these cases, and the postinfluenzal asthenia was much less marked

Hyperemic Phenomena —As previously pointed out, the severe epidemic cases showed a remarkable dusky erythema which usually persisted into convalescence, and which at times was followed by desquamation. This erythema was in no sense a simple flush, such as is seen in any fever, nor was it dependent on cyanosis, it appeared similar to certain rashes, such as those which occur in scarlet fever, serum disease, or after burns   The distribution, especially over face and neck, the intensity, the persistence after subsidence of fever, and the desquamation were its main features. A striking and characteristic appearance was also noted in the buccal cavity, consisting essentially of an intense hyperemia. Since the height of the epidemic these hyperemic phenomena have been present only to a very slight degree, in most cases there was no obvious change in the skin, although occasionally a slight dusky diffuse erythema was noted   The buccal cavity in the postepidemic cases shows usually only a slight diffuse reddening of the pharynx, pillars, and soft palate, with swelling of the lymphoid tissue on the pharyngeal wall   The appearance is similar to that seen in the epidemic cases, although much less outspoken   From the stand point of diagnosis the absence of localized inflammatory proc

esses in the throat seems of importance   There is never any circumscribed tonsillar or pharyngeal exudate or any swelling of regional lymph-glands in uncomplicated cases

General Physical Examination —As in the epidemic cases, gross local lesions were strikingly absent, in contrast to the fever and severe constitutional symptoms   In the uncomplicated cases, which made up the majority of the group, examination was negative except for the hyperemic phenomena described above   The lungs were clear and the spleen was not palpable

Complications —Bronchitis   and   bronchopneumonia   It seems of importance to distinguish sharply between the respiratory tract symptoms which are an integral part of the primary disease and those complications in the lung which while frequent and serious are still not an essential feature, although the primary "influenza" may directly predispose to their development   In practically every case at onset there is a diffuse hyperemia of the mucosa of the upper respiratory tract, which gives rise to conjunctivitis, obstruction to nasal breathing, with slight watery secretion, rawness of the throat, and dry tracheal cough, with slight mucoid sputum   These are essential features   Later a series of localized complications is prone to occur, all of which, however, seem to be secondary to the primary disease   Thus, otitis media, paranasal sinusitis, bronchitis, and, finally, bronchopneumonia may supervene   Such complications were, however, relatively infrequent in this series, in contrast to their incidence in large groups of individuals in close contact, as in some military camps, where secondary pneumonia was so frequent as to give rise to the impression that it was an essential feature of the disease   Bronchopneumonia was looked for in our cases with the utmost care, the diagnosis being based on cough, sputum, physical signs, and x-ray changes It was detected in 13, or 16 6 per cent , of the 78 cases   It must, of course, be recognized that the borderline between bronchitis and bronchopneumonia may be uncertain, and that small undetected foci of solidification may exist without being clinically demonstrable

Other complications were remarkably infrequent   Empyema

ccurred in two cases following pneumonia, and in one instance here was an acute sinusitis.

Leukocytes —In the postepidemic cases, as well as in the pidemic, leukopenia is the rule   The averages of the counts made on various days were as follows

Day	Count.
2	6650
3	6100
4	4900
5	6800
6	5100
7	4440
8	4200
9	7150
10	7600
11	7600

The lowest count was one of 1900 on the fourth day   In uncomplicated cases counts above normal were found only in two cases—14,000 (second day) and 13,000 (fifth day)

Leukopenia is, therefore, of great value as a diagnostic point in postepidemic as well as in epidemic cases

Fever —The character of individual temperature curves was similar to that of the epidemic cases   As emphasized previously, while the course of the curve shows nothing characteristic, the fever in uncomplicated cases is of strictly limited duration   Table I shows the day of disease on which the temperature became normal in the postepidemic cases compared with the epidemic cases

TABLE I

Day of disease on which temperature became normal	Postepidemic cases. Number	Postepidemic cases. Per cent.	Epidemic cases. Per cent.
1			
2	1	1 6	
3	2	3 2	3 9
4	8	13.0	8.5
5	13	21 0	14 2
6	9	14.5	14 0
7	14	22.5	25.0
8	11	18 0	16.0
9	4	6.5	12.5
	62		

Differential Diagnosis—Despite the confusion which exists, there are but few acute febrile conditions for which influenza can be mistaken During the period in which this series of cases was seen only 6 patients were admitted to the hospital in whom the diagnosis of influenza made at first turned out to be incorrect Four of these had acute follicular tonsillitis with localized tonsillar exudate, sore throat, pain on swallowing, cervical adenitis, and leukocytosis of from 12,000 to 15,000 The fifth patient had a local infection of the antrum of High more, from which a pure culture of pneumococcus was obtained, the leukocyte count was 13,000 The sixth had an acute otitis media with 32,000 leukocytes Acute rhinitis and coryza hardly bear a superficial resemblance to influenza. The relative insignificance of the constitutional symptoms, the local lesions, the indefinite duration, and the absence of leukopenia serve readily to differentiate the conditions It is true, however, that at a time when both influenza and mild respiratory infections are prevalent it may be difficult to tell whether one is associated with or sequent to the other Differential diagnosis between acute lobar pneumonia and postinfluenzal bronchopneumonia is usually easy The main points are as follows In the influenza bronchopneumonias one usually elicits a history of typical symptoms, which may improve after a few days, to be followed later by the more severe symptoms of the pneumonia. These cases showed a striking absence of dyspnea and tachycardia The tenacious rusty sputum of lobar pneumonia was not seen in any of the postinfluenza bronchopneumonias, but sputum, if present, was fluid and streaked with bright or dark blood The leukocytes are of special importance, as the leukopenia usually persisted even when pneumonia supervened This has been the rule in our cases, both mild and severe The physical signs in the lung are not diagnostic but sudden onset, rapidly followed by development of signs of lobar consolidation, with tachypnea, pleural pain, rusty sputum, and leukocytosis, speak strongly for acute lobar pneumonia

The cases which present the greatest diagnostic difficulty are the very mild or abortive ones There may be simply a

day or two of malaise, anorexia, slight sore throat, headache, or mild catarrhal symptoms That these cases may really be influenza seems clear from the subsequent development of prostration, with insomnia, tachycardia, or other symptoms

Diagnosis.—In summary, then, postepidemic influenza still presents a definite clinical picture As in the epidemic cases, there are striking constitutional symptoms, with at first few or no symptoms referable to the respiratory tract. The physical examination, apart from the hyperemia of skin and mucous membranes, shows nothing definite, in marked contrast to the severity of the symptoms Leukopenia is the rule during the active stage of the disease The temperature curves follow the same rules as in the epidemic cases. Except in extremely mild or abortive cases the diagnosis can usually be made with certainty

BIBLIOGRAPHY

1 Hewlett, A. W and Alberty W M   Jour Amer Med. Assoc., 1918, lxxi 1056.

2. Keegan J J Jour Amer Med Assoc. 1918 lxx 1051

3 Nurum J W Pilot, I., Stange, F H., Bonar B E   Jour Amer Med. Assoc. 1918, lxxi 1562

4 Fantus, B Jour Amer Med. Assoc. 1918, lxx 1736

5. Soper George A. Jour Amer Med. Assoc., 1918, lxxi 1899

6. Hall J N Stone M C. and Simpson, John C. Jour Amer Med. Assoc., 1918 lxxi 1986.

7 Christian Henry A. Jour Amer Med. Assoc. 1918, lxxi 1565

8. Strouse, S. and Bloch L. Jour Amer Med Assoc. 1918, lxxi, 1568

9 Hirsch, E. F and McKinney M   Jour Amer Med Assoc., 1918 lxxi, 1735

10 Friedländer A. McCord C Sladen F J Wheeler G W   Jour Amer Med Assoc., 1918 lxxi 1652.

11 Blanton W B., and Irons, E. E   Jour Amer Med. Assoc. 1918 lxxi, 1988

12. Synott, M J and Clark, E. Jour Amer Med Assoc., 1918, lxxi, 1816.

13 Ely C. F Lloyd B J Hitchcock, C I Nickson D H   Jour Amer Med Assoc., 1919 lxxii 24

14 Jour Amer Med Assoc. 1918, lxxi 2068

15 Bloomfield A. L. and Harrop G A. Jr   Bull Johns Hopkins Hosp 1919 xxx, 1

FROM THE GASTRO INTESTINAL CLINIC OF THE
JOHNS HOPKINS HOSPITAL

Notes on the Gastric Signs and Symptoms in Diseases Other
than Those of the Stomach

By THOMAS R. BROWN M D

Gastro-intestinal Disturbances in Metabolic Diseases and
Diseases of the Ductless Glands

By JOHN H KING, M D

The Role of Diet in Treatment of Digestive Diseases

By E H GAITHER, M D

Esophagoscopy

By E B FREEMAN, M D

CLINIC OF DR. THOMAS R BROWN

JOHNS HOPKINS HOSPITAL

NOTES ON THE GASTRIC SIGNS AND SYMPTOMS IN DISEASES OTHER THAN THOSE OF THE STOMACH

It is a trite but no less true saying that the greatest danger in modern medicine is the tendency toward intensive specialization. Every specialist, however honest he may be, is singularly prone to find symptoms and signs in most of the cases presented to him that may be regarded as within his own sphere, and to prove to his—and often also to the patient s—satisfaction that by the correction of these symptoms that greatest of desiderata—perfect health—will be obtained. And so ovaries are removed,

kidneys fixed in supposedly normal positions, appendectomies performed, sinuses drained, and tonsils dissected out, displaced uteri suspended and teeth extracted, and yet in many cases—to the patient's grief and the doctor's chagrin—perfect health comes but a step nearer, or sometimes seems even farther away, and the promised goal is still far away—intangible as any ignus fatuus   The reason for this can only be the striking overlapping of symptoms—their singular tendency to be referred to other organs or tissues than those pathologically affected, the ultimate solution of the problem with the optimum result to the patient, the discouraging of a too early entrance into any special field— the ideal, and in fact, the only safe specialist being one who has had early and broad training in general medicine, and, if possible, in general surgery before he commences to confine his activities to a more narrow special field, this is, indeed, the harder, as it is the longer path, but it is the only way out of the wilderness of modern ultraspecialization   There is perhaps no field in which the danger of regarding symptoms of disease as definitely due to pathologic conditions of the organs referred to is greater than in the digestive sphere, and it therefore seemed to us of interest and of real value to discuss briefly and often through illustrative cases of special interest, the gastric signs and symptoms met with in other diseases than those of the stomach itself   The field is so vast, gastric symptoms are so frequently met with as an expression of disease elsewhere, that we can but briefly touch upon many of the points even of special interest It is needless to call attention to the frequency of gastric symptoms, especially those of hyperchlorhydria, in cases of uncorrected refractive errors, especially astigmatism   Gould has contributed many articles of real interest to this subject, and has attempted to show that many of the great men of the past owed their digestive ill health to such a cause, Huxley, for instance, being a notable example   No less interesting are the nausea and vertigo so frequently found in diseases of the eighth nerve, while, on the other hand, the gastric symptoms met with in tonsillitis, sinusitis, and pyorrhea alveolaris are hardly to be regarded as referred symptoms through vagus or sympathetic

connections, but more as a definite expression of inflammatory changes of the gastric mucosa of toxic or bacterial origin

Let us briefly discuss the referred gastric signs and symptoms where the stomach itself, both as regards glandular apparatus, mucous membrane, and musculature is absolutely or almost absolutely normal, and where, therefore, signs and symptoms must be regarded as expressions of disturbed innervation of reflex or of toxic nature

DISEASES OF THE DIGESTIVE APPARATUS ITSELF

Not the least interesting chapter in this story of referred symptoms is that when signs and symptoms are gastric, but the disease is elsewhere in the digestive tract

In *chronic constipation*, for instance, the major symptoms may be those of an acid dyspepsia, but treatment directed to this condition alone will be singularly unsuccessful, while the gastric picture may clear up as if by magic if the underlying intestinal condition is radically attacked, for, after all, in the vast majority of cases the gastric hyperchlorhydria and achylia are but expressions of extragastric diseased conditions, and to be satisfied with them as diagnoses is quite as pathetic as writing as a case diagnosis headache or jaundice or neuralgia or even endocrinopathy

If we have a high grade of intestinal stasis due to ptosis, atony, chronic appendicitis, etc , the gastric symptoms may be more stormy—we may have periodic attacks of the most severe symptoms—nausea, vomiting, gastric pain, anorexia, etc., associated with profound prostration, and yet the stomach itself may be an absolutely normal organ Are the attacks met with in these cases to be regarded as anaphylactic in nature or as a colossal vagotony? Whatever the explanation, the theory of auto-intoxication unquestionably explains best the symptom complex presented Is it a toxin normally present but in excess, is it due to the insufficiency of the liver and other portions of the protective mechanism, is there a marked overgrowth of the Gram positive proteolytic anaerobes, or is there a perversion of ferments or intestinal excretions? It is very striking

what slight changes in molecular constitution are necessary to convert the normal amide bases met with in digestion of the proteins into products of the greatest toxicity, as, for instance, the change from lysin to cadaverin, or arginin to putrescin.

When *true obstruction* occurs the picture is even more interesting Let us quote then briefly from our notes of a case seen a few months ago, a man whose only complaint was severe epigastric pain, nausea, and vomiting, which he, following alas, the explanation of all patients and many physicians, ascribed to improper diet   A physical examination revealed a very small incarcerated inguinal hernia of the right side with absolutely no local symptoms, and with its immediate surgical treatment the gastric symptoms disappeared as if by magic

It is superfluous, of course, to call attention to the many cases of *acute appendicitis* in which the only symptoms of the acute inflammation in this organ with its associated local paresis of the nearby gut are purely gastric—epigastric pain and tenderness, nausea, vomiting, and even muscle spasm over the pyloric region—and here, again, a wrong interpretation of the underlying cause and its consequent treatment by purgatives often lead to most deplorable results

The frequency with which early *intestinal neoplasms* have as their only symptoms a gastric syndrome singularly like that of gastric ulcer with associated hyperchlorhydria is only too well known, and the finding at operation or autopsy of an inoperable carcinoma, often absolutely impossible of diagnosis in its early stages even with most careful x-ray and stool studies, comes as a profound shock to the belief in our diagnostic skill   We recall only too well a case of rather vague symptoms in its early stages, but where finally all the symptoms crystallized into the typical picture of pyloric ulcer, which was "confirmed" by x-ray studies made by two most capable radiologists, and where because of persistence of symptoms surgery was had recourse to, and an inoperable carcinoma of the sigmoid found, with a normal stomach

To us one of the most interesting findings has been the gastric picture met with in *cholelithiasis* or even in cases of chronic

cholecystitis and pericholecystitis with adhesion formation In one case we see the typical picture of a chronic functional dyspepsia—fulness and discomfort after meals, and especially that bane of the gastro-enterologist—gas in incomprehensible amounts, often, of course, but an expression of aërophagy, in the other a picture so like that of gastric cancer with its lack of appetite, loss of weight, etc., that even with the persistent absence of occult blood and the negative roentgenograms, we often are in doubt, and only the operation definitely determines that we are dealing with a case of gall-stones or chronic cholecystitis with no local manifestations

In both of these types—types especially prevalent among fat women after early middle life—our studies have shown that an achylia, or at least an achlorhydria, is the rule—although, of course, in *acute* gall-stone colic hyperchlorhydria is not at all unusual In gall bladder disease these referred gastric symptoms, undoubtedly of vagal origin, are peculiarly interesting in that they have a definite cardiac equivalent—all the signs and symptoms of a cardiopathy being quite often found in this group of cases—symptoms which entirely disappear, with a realization that the heart trouble was functional and not organic, after the appropriate surgical treatment of the gall bladder And so we might go on almost indefinitely referring to cases of great interest in duodenum, small and large intestine, and pancreas—singularly interesting examples being the gastric pictures in both acute and chronic pancreatitis, as well as carcinoma at the head of the pancreas—but space does not permit, as we must briefly note the confusing gastric picture so often met with as the main or often the only symptom of diseased conditions in other organs than those of the digestive tract

DISEASES OF THE PELVIC ORGANS

In our experience the most interesting gastric manifestation of disturbance in this sphere is the occurrence of attacks of periodic and extremely severe nausea and vomiting in cases of marked retroflexion of the uterus, with no local symptoms, and yet with complete disappearance of the gastric symptoms after the sus-

pension of the uterus   We have had 3 such cases within the past year, all previously regarded as cases of pyloric ulcer, and obviously resistant to the usual treatment

Another interesting picture is that of the acute gastralgias with nausea and vomiting met with in cases of ovarian cysts with twisted pedicles—always extremely difficult to diagnosticate, and frequently regarded as cases of acute appendicitis with only upper abdominal symptoms

INFECTIOUS DISEASES

We have been singularly interested in the gastric manifestations met with in the acute and chronic infectious diseases, notably *typhoid fever*, *tuberculosis*, and *syphilis*   Certainly the more one studies *pulmonary tuberculosis*, the more one realizes the protean modes of onset met with, and one of the commonest is where the symptoms are truly gastric or gastro-intestinal— —a functional atonic dyspepsia in one case, and this is the commonest in our experience, or symptoms of hyperchlorhydria, or nausea with or without vomiting, or, in other cases, intestinal dyspepsia often with diarrhea   It is surprising how many cases come to our clinic complaining only of gastro-intestinal symptoms and without cough or dyspnea, chills, or sweats, where the physical examination shows the gastro-intestinal tract to be fundamentally sound, but the lung definitely involved

After *typhoid fever* a certain proportion of the cases shows a dyspepsia which careful investigation demonstrates to be associated with an intractable achylia, and in a considerable number of such cases it has taken many months of treatment with acid and appropriate diet before the normal gastric findings are again met with, that they do return to normal, however, furnishes suggestive if not absolutely conclusive evidence that the condition is purely functional

In *syphilis* we may meet with a protean gastric picture, notably in the tertiary stage, but here the changes are of organic, not functional, nature, but in the parasyphilitic tabes dorsalis we meet with perhaps its most interesting manifestation in the gastric sphere—gastric crises on the one hand, usually re

garded as attacks of gastric ulcer, or gall-stone colic, or acute appendicitis, and on the other with what we have regarded as its motor equivalent—periodic attacks of intractable vomiting

In the *arthritides* of infectious origin achylia is the rule, although in our experience acid therapy is not well borne, and often, strange to say, tends to aggravate rather than alleviate the joint symptoms, although we believe Goldthwaite and others still use lactic acid in the shape of buttermilk in large amounts in this group of cases

DISEASES OF METABOLISM AND OF THE ENDOCRINE GLANDS

The gastric findings in these cases will be discussed at length by Dr King in this volume, and so we will merely call attention in passing to the frequency with which absence of hydrochloric acid is met with in *chronic gout*, which has led many, notably Von Noorden, to substitute an acid for an alkaline therapy in this disease, and the frequency with which an achylia is met with in both *hyperthyroidism*, Graves' disease, and the reverse condition—*hypothyroidism* or myxedema. Certainly, some of the so-called nervous diarrheas represent early manifestations of an overactive thyroid gland, but why the achylia met with in myxedema is usually associated with an intractable constipation is more difficult to explain

INTESTINAL PARASITES

It is surprising with what great frequency cases of intestinal parasitism present only gastric symptoms Here, again, the gastric findings are usually a diminution or complete absence of hydrochloric acid We well remember a case seen by us a few years ago—a physician from Georgia, about fifty years of age, in whom loss of weight, increasing anemia and cachexia, lack of hydrochloric acid in the gastric contents, and persistent, though faint, traces of occult blood in the stool made one extremely suspicious of gastric cancer The stool examination made with the greatest care did not, at first, show embryos, parasites, or ova, but one was struck by the enormous number of Charcot-Leyden crystals in the stool and the blood showing

a marked eosinophilia—over 40 per cent in this case—made one feel sure that the condition was due to an intestinal parasite. Repeated doses of thymol followed by purgatives finally were rewarded by the finding of ova and embryos of uncinaria—the parasite most loath to leave its intestinal home—and drastic treatment finally led to a complete cure The case was a singularly illuminating one, and illustrates the importance of thorough microscopic studies of stool and of blood in all doubt ful cases

PERNICIOUS ANEMIA

The association of anemia, nausea and vomiting, and gastric achylia is the classical picture of a pernicious anemia, and every clinician knows the extreme difficulty often met with in dif ferentiating it from gastric cancer Careful differential blood studies, radiograms—often a frail reed, however—and thorough stool studies with persistent occult blood in the one, absence of occult blood in the other, help in this differentiation, though in some cases only the autopsy findings reveal the diagnosis

THE PSYCHONEUROSES

Functional disturbances—especially along the course of the vagus—are so common a manifestation of the irritable weak ness of the psychasthenic or neurasthenic state that they hardly need be mentioned Every clinician knows that profound digestive disturbances—anorexia, nausea and vomiting, acid dyspepsia, gastralgia, etc —may follow sudden or prolonged shock or strain or emotional outbreak and every animal ex perimenter knows how easy it is to produce a complete temporary cessation of the motor and secretory functions of the stomach by fear, anger, excitement, etc   There are no more interesting group of cases than the so-called psychogenic or neurogenic gastrogenous diarrheas, for example, of which we see many cases every year   Let us quote briefly the history of one such case—a strong, healthy, Irish boy—valet to an irascible master who was subject to violent outbursts of temper   After one such outburst, during which the boy really feared for his life, he de veloped a diarrhea which still persisted when we saw him several

years later An achylia was found, and the symptoms rapidly yielded to hydrochloric acid therapy, which, however, could not be discontinued without a reappearance of the diarrhea In this case there was after a number of months of acid therapy a return of the normal gastric secretions, but this is a rare finding, as in most cases the achylia persists Obviously, in this case the cause of the achylia was a complete blocking of the vagal path with its stimulating impulses as a result of overpowering fear Here we have functional derangements in a maximum form, but we must never forget that even every organic lesion is accompanied by some functional disturbance, and the determination of the relative rôles played by organic and functional changes is one of the many fascinating problems that the clinician must solve if he is to expect success.

CARDIOVASCULAR DISEASES

A very wise clinician once said, "When a patient complains of indigestion with no apparent cause, always think of the possibility of beginning myocardial insufficiency, when he or she complains of cardiac symptoms, always realize the probability that these symptoms are of gastric origin " This peculiar overlapping of symptoms in diseases of the heart and of the stomach is, of course, partly due to their close anatomic juxtaposition, partly to their similar nerve supply Perhaps the most striking example of all is the great frequency with which cases of pure angina pectoris present as their main—sometimes apparently as their only—symptom, the typical picture of an acute indigestion, an error of diagnosis singularly dangerous as evidenced by the number of deaths from so-called "acute indigestion," the vast majority of which are atypical cases of angina pectoris or of cardiac dilatation, a very small minority true cases of acute dilatation of the stomach, and an occasional case representing a true abdominal angina, due in all probability to a claudication or partial cutting off of local blood-supply associated with a sclerosis of certain of the arteries within the abdominal cavity We remember very well one of these cases in which periodic paroxysms of the most violent epigastric and right hypochondriac

pain with exquisite local tenderness made one think of gall stone or perforated gastric ulcer or acute pancreatitis, but in which the subsequent course of the case proved beyond peradventure that we were dealing with a case of arteriosclerosis of the mesenteric vessels with attacks of abdominal angina

Perhaps of equal interest are those cases of just beginning myocardial incompetency in which the only signs and symptoms are those of a mild functional dyspepsia—gas, fulness, feeling of pressure after meals, slight anorexia, etc   In cases where the past history has furnished probable causes for myocardial change, especially in the moderately old and very fat, this possibility should always be taken into consideration, and a short course of very small doses of digitalis may clear up with surprising rapidity symptoms which have proved absolutely refractory to treatment directed to the stomach alone, and rightly so, because the underlying cause was not being attacked—only the symptoms produced thereby   In more marked cases of myocardial decompensation, digestive disturbances are, of course, very common, but here the picture is a simple one, as the symptoms simply represent the disturbances due to the chronic passive congestion and the usually associated gastric achylia, a picture very similar to that met with in parenchymatous nephritis

DISEASES OF THE KIDNEYS

It is common knowledge how frequently pyelitis and nephrolithiasis are mistaken for gastro-intestinal diseases, notably acute appendicitis and gastric ulcer, and we have already touched upon the functional disturbances of the stomach met with in chronic parenchymatous nephritis   In interstitial nephritis and in tuberculosis of the kidney the picture may be even more interesting   Two cases we especially remember—one in which the progressive anemia and loss of weight, the almost complete anorexia with persistent nausea and periodic vomiting and the gastric achylia had led to a diagnosis of gastric carcinoma, but which a very thorough urinary study showed to be a case of tuberculous nephritis, the other, with almost an identical picture and with the same diagnosis, which urinary studies,

functional tests, and the subsequent history proved to be a case of interstitial nephritis, where eye symptoms, hypertension, and cardiac hypertrophy had not yet made their appearance, and where the only symptoms were those met with in the gastro-intestinal sphere

We might go on almost indefinitely reciting cases of diseases in various portions of the body where the true nature of the underlying pathologic condition was entirely masked by symptoms referred exclusively, or almost so, to the stomach or intestine   We have shown enough, we feel, to prove the point we made at the beginning of this short article, namely, that there is such an overlapping of symptoms in diseases that the only safe specialist is the one who is not a true specialist, but is the one who, in the more intensive study of special organ or tissue or method, has not forgotten the art and science of general internal medicine, and never overlooks the fact that no organs or tissues can be considered separately, but that each is but a part of the whole, and all are indissolubly linked together by nervous and by vascular connections   Only by a realization of this and by an appreciation of its inevitable consequences can a correct diagnosis be made and rational therapy be instituted

CLINIC OF DR JOHN H KING

JOHNS HOPKINS HOSPITAL

GASTRO-INTESTINAL DISTURBANCES IN METABOLIC DISEASES AND DISEASES OF THE DUCTLESS GLANDS

INTRODUCTION

THE gastro-intestinal tract through the exercise of its manifold activities exerts an important influence upon the normal functions of the body Disturbances in the normal workings of the stomach and intestines may be primary, resulting from changes originating directly in the gastro-intestinal tract, or secondary, as a consequence of disease processes elsewhere in the body

There are several primary functions of the gastro-intestinal tract which have an influence on disease processes located in other organs of the body

I The Secretory Function —(a) The increased secretion of

hydrochloric acid is apt to be associated with pyloric spasm and, later on, gastric atony   Furthermore, hyperacidity frequently interferes with proper ingestion of food, because it may cause painful sensations and even vomiting during digestion

(b) Diminution in the secretion of hydrochloric acid results in the food reaching the intestines in an insufficiently prepared state and also allows a decomposition process to be set up in the stomach, with the resulting clinical symptoms of flatulence, epigastric pressure, and belching of gas   When the condition goes on to complete absence of free hydrochloric acid, the emptying time of the stomach is greatly accelerated, giving rise often to a feeling of emptiness shortly after eating, and epigastric unrest

II The Motor Function —Increase in the motility of the stomach and intestines may be associated with an obstinate and very profuse diarrhea, which, occurring in association with some disease in another part of the body, may affect the prognosis very critically

Decreased motility of the gastro-intestinal tract, particularly in extreme grades, sufficient to produce stagnation, can give rise to vomiting, which may lead to a considerable degree of exhaustion and malnutrition

III Decomposition, in the stomach and intestines, is prone to upset gastric and intestinal digestion   Decomposition of the gastric contents is often associated with feelings of giddiness, languor, and headache, a condition called by Trousseau gastric vertigo   Distention of the stomach and intestines may give rise to cardiac distress amounting to actual cardiac dyspnea   With extreme dilation of the stomach, associated with severe grades of decomposition of the stomach contents, the clinical condition called gastric tetany by Kussmaul may occur

IV Inflammation of the stomach and intestines, particularly those of an acute nature, have a very unfavorable influence upon disease processes   The occurrence of an acute enteritis, in the course of any critical disease, is always looked upon with grave forebodings

Disease processes elsewhere in the body often have a marked

secondary effect upon the gastro-intestinal tract The derangements of the stomach and intestines, though a late development in the clinical picture, may quickly become the dominating features

The symptoms and signs of a disease entity may be so clear and striking that the diagnosis is at once apparent and certain The clinician's attention is perhaps then focused exclusively on the main disease process, and important secondary symptoms, which indicate the progress of the disease, are neglected Furthermore, symptoms which have apparently little significance in themselves are often the means of directing the observer's attention to a serious ailment of the body Perhaps no domain of the body has more influence over the progress of disease, or conversely, is more influenced by morbid process of the body, than the gastro-intestinal tract It is therefore important to analyze carefully the signs of derangement of the stomach and intestines, seeking to find out if they point to some more obscure disease, as well as to appreciate their prognostic significance upon a disease process already well established

The gastro-intestinal tract is the great means of bringing sustenance to the body, and eliminating useless and harmful products from the body Its normal activity is essential for the good health of the individual, and consequently it plays an important rôle in practically every disease As long as it functions normally and supplies nutriment to the body, it helps to combat disease When its functions break down, then disease ravishes the body more rapidly

It is the purpose of this clinic to call attention to some of the gastro-intestinal symptoms and signs in the diseases of metabolism and the endocrinopathies

GENERAL METABOLIC DISEASES

Diabetes —In this disease, where the problem is largely that of maintaining the patient in good nutrition upon a selected diet, special attention must be paid to any derangement of the gastro-intestinal tract.

Gastric Symptoms —Polyuria and polydypsia do not neces

sarily predispose to affections of the stomach, especially in the early stages of diabetes   The stomach may function normally in spite of the tremendous amounts of food and liquids that it is called upon to handle   The gastric acidity shows no peculiarity in its behavior, the variations are within the normal limits

In the later stages of diabetes, when the patient is debilitated and coma is threatening, gastric motility is often very much diminished, with resulting atony and stagnation, loss of appetite, fermentation, and vomiting   A tendency to hyperchlorhydria, associated with burning sensations in the epigastrium, hyperesthesia, and feeling of pressure in the region of the stomach is often associated with the later stages of this disease

Intestinal Symptoms —A predisposition to constipation is the rule in diabetes, while diarrhea is much less common. Constipation comes on very easily in this disease, when the carbohydrates, especially bread, are removed from the dietary

Diarrhea is apt to supervene on a vegetable and fat diet. It is not always an evidence of catarrh of the bowel, as it often comes on in a bizarre form, with a sudden onset and equally sudden cessation, like a nervous diarrhea   On the other hand, diarrhea may result from a true catarrh of the bowel and is a serious symptom, both because it interferes with proper nourishment and often ushers in coma

When the diarrhea in diabetes mellitus results from a true enteritis the movements are semisolid, often contain considerable mucus, and continue for a long while   When the diet is responsible for the increased evacuations there is associated distention, abdominal cramps, with watery evacuations, followed by almost immediate relief   If disturbances in the external secretion of the pancreas are responsible for the diarrhea, the bowel movements contain an excess of fats and are strikingly offensive

In general, the resorption of food from the intestinal tract is good, and there is no increase in fats or carbohydrates in the feces   When the external functions of the pancreas are involved as well, then there may be large amounts of undigested fats and proteins in the feces   Stagnation in the bowels with

decomposition exerts a deleterious effect upon the cause of diabetes, and to it is ascribed by some the onset of coma diabeticum

Coma Diabeticum —This most fatal complication of diabetes is often associated with striking gastro-intestinal symptoms It may be ushered in by an acute attack of nausea and vomiting, followed rapidly by onset of coma, or an acute attack of true catarrhal enterocolitis with marked diarrhea may precede the coma. Both of these complications are serious, since they make very difficult the maintenance of the patient's nutrition during the period of coma

On the other hand, a period of marked constipation may be a forerunner of coma. Here nutrition is not interfered with so seriously, but to the deleterious effects of retained decomposition products and their absorption is ascribed the onset of coma Diarrhea is in no sense a necessary accompaniment of coma It is lacking in at least one-half of these cases On the other hand, long periods of constipation in diabetes must be viewed with care, as they undoubtedly predispose to coma

Though there are no specific gastro-intestinal disturbances associated with diabetes, any serious derangement of the functions of this tract may influence the course of this disease very deleteriously It is therefore important to recognize early signs of stagnation or inflammation of the gut, particularly for the purpose of discerning the onset of coma and taking precautions to ward off this most fatal complication These conditions though even of a mild degree, must be considered serious and relieved as promptly as possible, since their persistence is a constant danger to the patient

Gout.—The gastro-intestinal symptoms of gout may be very insignificant, the disease running a long course without anything more than slight constipation and flatulence However in other cases, a tendency to severe and uncontrollable diarrhea exists, which may be associated with nausea and anorexia These symptoms are often the precursor of the gouty paroxysms

A deficiency of hydrochloric acid secretion is common in

gout, but it is not characteristic Such a condition is generally due to a complicating gastritis or general manition In the later stages of gout achylia gastrica may supervene

There is often a definite tendency to intestinal putrefaction in gout, with a high elimination of nitrogen in the feces, without a high percentage of fat in the stools, indicating an increased excretion of nitrogen rather than a diminished absorption.

In retrocedent or suppressed gout, a term which is applied to serious internal symptoms coincident with a rapid disappearance or improvement of the local signs, very severe gastro-intestinal symptoms may develop, consisting of pain, vomiting, diarrhea, and great depression Such an attack may result fatally

Obesity, resulting from overindulgence in food or alcohol, is particularly prone to be complicated by disturbances of the stomach and intestines

The continued strain upon the tone of the stomach caused by overloading with food and liquids results in the end in gastric atony, with its attendant train of symptoms—flatulence, epigastric pressure, and early feeling of satiety

Many cases of obesity develop a severe type of diarrhea associated with cramps in the lower part of the abdomen, followed by two or three watery movements and expulsions of considerable offensive gas The bowel movements may contain much mucus and be as frequent as five to ten movements daily

Another type of severe diarrhea may develop from constipation, resulting from the accumulation of feces, forming hard scybalous masses, which excite frequent movements, or form stercoral ulcers which reflexly stimulate the movements of the bowel

The most severe and intractable diarrhea is that induced by fatty degeneration of the liver, which may accompany severe grades of obesity

In the anemic form of obesity, which occurs mostly in women, and is associated with anemia often of the chlorotic type, gastrointestinal symptoms may be prominent The appetite is generally poor and, peculiarly, carbohydrates are preferred to proteins by the patient The tongue is furred and the breath often

foul Intestinal flatulence associated with constipation is common Diarrhea is less frequent, but may be severe, due to an acute or chronic catarrhal inflammation of the bowel

DISEASES OF THE DUCTLESS GLANDS

The Endocrine Glands —The gastro-intestinal tract shares, with the rest of the organs of the body, in the secondary effects resulting from disturbances in the functions of the ductless glands Some of the endocrine glands have a very considerable influence on the gastro-intestinal tract both through their effect upon its secretory functions as well as by influence on the autonomic and vegetative nerve fibers of these organs Conversely, derangements of the gastro-intestinal tract react upon the ductless glands, particularly when the latter are functioning abnormally An attempt will, therefore, be made to call attention to some of the more important clinical disturbances of the gastro-intestinal tract, associated with derangements of the ductless glands.

Diseases of the Thyroid —Disturbances in the normal functioning of the thyroid gland are often strikingly associated with gastro-intestinal symptoms In fact, the latter may be so pronounced as to completely obscure the fundamental disturbances in the thyroid

The thyroid gland possesses the properties of stimulating secretion, motility, and accelerating the body metabolism All these factors have an influence upon the gastro-intestinal tract When the thyroid is stimulated to overactivity the reaction on the gastro-intestinal tract is striking Conversely, when the gland is sluggish, a reaction in many ways diametrically opposite is produced on this tract

Exophthalmic Goiter —In this disease, associated with hyperactivity of the thyroid gland, the stomach is apparently less influenced than the intestines. However, there may be a complete cessation in the secretion of hydrochloric acid, resulting in practically an achylia gastrica, and the motility of the stomach may be greatly increased These changes result often in an empty feeling in the stomach after eating, and again, in a striking diarrhea

Diarrhea may be one of the most frequent and annoying symptoms of this disease   "It may usher in the disease, appear at any time, be transitory, periodic, or remain permanently, and greatly increase the severity of the disease   The stools may even escape involuntarily "

"On the other hand, the diarrhea may be of sudden onset, and appear at the crises of the disease when the tachycardia, ocular, and other manifestations are most pronounced   This may occur both in the early and late stages of the disease "

The movements are fluid, bile-tinged, and often contain whole food fragments a few hours after same have been eaten, indicating an increased peristalsis of the stomach and intestines, in addition to impaired digestion

This frequent diarrhea may be so prominent and the thyroid signs so obscure that only very careful physical study and pharmacodynamic tests enable the clinician to demonstrate that the diarrhea is dependent on hyperactivity of the thyroid

Again, the diarrhea takes the type known as the nocturnal diarrhea, characterized by a number of passages of the bowel rapidly following one another in the early morning   These patients often have a ravenous appetite, eat much more than they can digest, and later develop true enterocolitis with mucus in the stools

In very acute types of Basedow's disease nausea and incessant vomiting may complicate the diarrhea   Many of the so-called nervous diarrheas are secondary to an overfunctioning of the thyroid gland   The diarrhea of exophthalmic goiter has been referred to irritation of the vagus nerve by Eppinger and Hess and by others to the fact that an absence of free hydrochloric acid in the stomach allows the pylorus to remain open, and the food passes rapidly into the intestines in an improperly prepared condition   There results an excessive stimulation of the intestines with a rapid emptying, culminating in frequent watery movements containing undigested food particles   A fatty diarrhea with lowered carbohydrate tolerence has been described   This has been explained by some author on the basis of inhibition of the pancreas by the hyperactive thyroid

The beneficial therapeutic results from acid medication and dietary are often striking in the diarrhea occurring in hyperthyroidism

Myxedema —Diarrhea is extremely uncommon in this disease, in fact, a rather obstinate constipation generally exists   This diametrically opposed reaction of the gastro-intestinal tract seems to indicate a specific action of the thyroid gland in these cases   This is further substantiated by the fact that the diarrhea generally clears up with the reduction in the gland surgically

Diseases of the Pancreas.—Disturbances in the normal activity of the pancreas may be associated with pronounced gastro-intestinal symptoms   The most striking clinical picture is that occurring in conjunction with acute hemorrhagic pancreatitis   There is sudden violent colicky pain localized in the upper part of the abdomen.   Then follows nausea and vomiting, with eventually collapse   The abdomen becomes swollen and tense   Usually there is constipation   Collapse may come on and the patient die as early as the second to fourth day of the disease

Impairment in the external secretion of the pancreas may cause disturbances in the digestion and absorption of the fats and proteins   The clinical signs of such disturbances may be striking, while the symptoms may be only slight

Disturbances of the fat digestion result in insufficient absorption of fat, so that a greater percentage than normal is present in the feces   The stools may be oily, like butter, or of a gray asbestos-like color   The bulk of fecal matter is greatly increased

This condition may be associated with considerable diarrhea, with resulting loss of strength, or it may persist for years without definite impairment in the health of the patient

Disturbances of the protein digestion result in a marked increase in the percentage of protein in the feces.   The stools may contain numerous undigested muscle fibers   There results eventually considerable loss of weight on the part of the patient due to the lessened nutrition which he obtains from his food

A striking impairment in the lipolytic and tryptic ferments

of the pancreatic secretion may be associated with the clinical condition of chronic pancreatitis   In the symptomatology of this disease the gastro-intestinal tract may play a conspicuous part   Dyspeptic disturbances are often a prominent feature, consisting of anorexia, discomfort from flatulence, offensive eructations, heart-burn, and nausea   Frequently there is a distaste for fats and meats   In the early stages of the disease constipation with flatulency is common, while in the advanced stage frequent bulky bowel movements, pale in color, offensive and oily, predominate   Very marked wasting of the patient is often a prominent symptom   There may be distinct tenderness in the epigastrium with some fulness above the umbilicus

Adrenals —*Addison's Disease* —The gastro-intestinal symptoms in this disease are various   In the early stages of the disease patients complain of nausea, pressure on the stomach, ' and sometimes epigastric pains with vomiting   There is in the later stages generally a decrease in, or absence of, hydrochloric acid formation and ferment production   Diarrhea may alternate with constipation   Toward the end of the disease the diarrhea may occur in crises with great violence, without obvious cause, and be associated with spasms of the calves of the legs It takes the form of frequent watery discharges with colicky pains, and may lead to rapid collapse, delirium, and coma   In the terminal stages there may be incessant vomiting   The abdomen is generally retracted and the abdominal walls tense, the pulse is small, and the clinical picture suggests that of peritonitis

The Parathyroid Gland —*A parathyrosis* —Of the clinical symptoms of insufficiency of the parathyroid gland, perhaps the most striking is tetany   With this condition slight or severe disturbances of the function of the gastro-intestinal tract are frequently associated   In one type the tetany develops in patients who have been sick for a long time with gastric and intestinal disorders, especially those producing high-grade stagnation of the stomach contents

In another type the gastro-intestinal symptoms occur at or after the outbreak of the tetany   There is hyperexcitability

of the stomach musculature, increased secretion of the gastric and intestinal glands, and a pronounced "stratification" of the gastric contents

In still another type the gastro-intestinal symptoms may occur later and be intensified by the occurrence of tetany

The results of detailed studies show that in the acute stage of tetany the gastro-intestinal tract may show symptoms of hyper-excitibility and heightened tone, reaching eventually to a spastic condition   Associated with this is usually an increase in the secretory activity of the tract.

Diseases of the Pituitary —Disturbances in function of the pituitary gland are not particularly associated with gastro-intestinal symptoms   Those which do occur are allied with hyperactivity of the gland function, as evidenced by the clinical condition of acromegaly   The gastric and intestinal symptoms in this disease are vague, consisting of increased appetite and thirst, constipation, and various ill-defined dyspeptic disturbances.

Secondary pressure effects from tumor of the hypophysis may cause cerebral vertigo, in which clinical picture nausea, with explosive, projectile vomiting may be very prominent.

Diseases of the thymus and pineal glands are not associated with any definite gastro-intestinal symptoms

The thymus gland, through its correlation with the thyroid in hyperthyroidism, might be considered to play a part in the gastro-intestinal symptoms of Basedow's disease, but the association is, to say the least, a remote one

Disturbances in the function of the pineal gland are likewise not often accompanied by gastro-intestinal disturbances Only the local effects caused by enlargement of the gland with pressure upon the neighboring cerebral structures cause the gastro-intestinal symptoms   Here cerebral vomiting may be a striking symptom   The trophic changes produced by the gland are not associated with derangements of the stomach or intestines

Discussion.—Though there are no specific disturbances of the gastro-intestinal tract associated with either the diseases of

metabolism or the ductless glands, except it be the diarrhea of hyperthyroidism, still a sufficient number of derangements of this tract do occur to make it of interest to bring them together for their diagnostic and prognostic importance

When the etiologic chain of these obscure diseases is better unravelled, and the pathologic interrelationships more clearly understood, it may be that the rôle of the gastro-intestinal tract in these diseases will be clearer to the clinician Until then it will perhaps have served a useful purpose to have gathered together the fragments of our knowledge on this subject in preparation for future clinical correlation

CLINIC OF DR E H GAITHER

Johns Hopkins Hospital

THE RÔLE OF DIET IN TREATMENT OF DIGESTIVE DISEASES

Diet is undoubtedly the most potent single therapeutic measure we possess in dealing with digestive diseases   The application of drugs is not to be compared with food properly prepared and given in a suitable manner, namely, essential caloric value combined with physical characteristics which will both tempt the patient and stimulate the psychic secretion of gastric juice, and at the same time so prepared (in the way of liquids, purées, etc.) that the minimum burden of physical and chemical endeavor is placed upon the damaged organs   One cannot emphasize too strongly the great importance of serving food which will cause the patient to anticipate with pleasurable expectancy the coming of the diet tray   Daily in our work are we more and more convinced of the efficacy of the versatility of nurse or doctor in their suggestion or preparation of food, playing a predominant rôle in restoring digestive organs and patients to vigorous physical fitness, after the former have been wrecked by injudicious eating and drinking so much in vogue today, which, in many cases, lead to a true anorexia or sitophobia, because of the abuse of what was once supposed to be an "iron stomach "

One must necessarily have a full understanding of the mechanical factors and physiology of digestion, also a fundamental conception of caloric value and chemical properties of the various foods, and last, but not least, digestive pathology   Without these primary sources of knowledge it obviously will not be pos-

sible to scientifically or practically apply dietetic principles in an intelligent and helpful manner

It may be well to first discuss the physical characteristics of various foods first, liquids, second, gruels, third, soft foods, fourth, solids

Of the liquids, it may be well to divide them into non stimulating (*a*) and stimulating (*b*) varieties Of the former, we have—

(*a*) Milk, solution of egg-albumen, whey, cream, butter milk, koumiss, kephir, cocoa, chocolate, malted milk, cream soups, *i e*, asparagus, celery, pea, etc

(*b*) Beef extracts, beef juices, soups, bouillon, and broths of various kinds (chicken, beef, oysters, clam, vegetable) Cof fee and tea

Possibly it is best to speak of fruit juices as mildly stimulat ing

Those foods which are next in consistency, tending toward the soft or solids, would consist of the watery carbohydrates, prepared from the finely divided cereals, or purée of vegetables, *i e*, oatmeal, cream of wheat, wheatena, hominy grits, corn meal, malted milk, rice, macaroni, spaghetti, potato, vermicelli, spinach, asparagus, peas, cauliflower, beans

Soft foods consist of cereals not diluted with milk or water —oatmeal, cream of wheat, wheatena, farina, hominy grits, Pettijohns, *purées* of spinach, peas, beans, cauliflower, asparagus, onions, potatoes Purée of fruits—prunes, peaches, apricots, apples, etc

Macaroni, spaghetti, vermicelli, and rice in their usual state may be considered soft articles of diet

Tapioca, blanc mange, Spanish cream, gelatin, ice-cream, jellies, honey

Eggs prepared in various styles

Pulp of orange or grape-fruit

Butter, cream cheese

As solids in the strict sense we may consider poultry, fish, game, meat, potatoes, string beans, cauliflower, baked squash, beet greens, Brussels sprouts, turnips, carrots, cabbage, peas,

beans, celery, cucumbers, lettuce, parsnips, watercress, fruits, bread, cheese, nuts

Now that we have specific knowledge concerning the various classes of foods—i e, liquids, gruels or mushes, soft and solid articles of diet—it will be of interest to consider other properties, because there are certain fundamental principles which must be thoroughly understood before we can acceptably prescribe the various articles enumerated above to certain and specific pathologic entities of the digestive tract.

While we have not included water as a food, yet its value is nevertheless thoroughly appreciated relative to the general and specific needs of the body. Therefore it will not be amiss to discuss briefly its rôle regarding the digestive tract. Many opinions have been advanced regarding the efficacy of drinking large or small amounts of water, but it seems that the wisest procedure is to consume moderate amounts (about 6 glasses) during the day, and, in addition (and this seems a point worth emphasizing), the intake should be evenly distributed. Large amounts at one time are certainly detrimental. A transgression of this last point is especially to be avoided in degenerative processes affecting the vascular system.

Always bear in mind the fact that practically no water is absorbed by the mucous membrane of the stomach, and, if the stomach is functioning normally, a pint will be evacuated in from one half to three-quarters of an hour. The former point remembered will tell us why the patients with gastric stenosis bitterly complain of intense thirst. If taken in moderation water certainly does not retard digestion, in fact, it may be helpful inasmuch as it is a slight stimulant of gastric secretion, and also it may be of some value in softening food. As to its relationship to absorption, one would think, if anything, it would assist and not hinder.

Regarding mineral waters, especially those impregnated with carbonic acid gas, one may say if taken in moderation they are helpful, due to the promotion of chemical processes of digestion, because of an early and abundant secretion of gastric juice, also it may be helpful from a mechanical standpoint due

to the movements of the stomach being accelerated by the carbonic acid   These waters should not be used where heart affections are present, or where the appetite is already depressed.

Milk is one of the most valuable and important articles of diet which we possess   Because of the fact that it curdles with the formation of clot upon entrance into the stomach, many are inclined to class it with the solids, however, our personal experience (with few exceptions) has been so successful when using it in the sense of a liquid that we prefer not to look upon it in the ordinary sense of a solid   We are in agreement with Pawlow's statement that in proportion to the amount of nitrogen milk contains it requires for its digestion a weaker gastric juice than any other food   Hence the secretory work required of the stomach for its digestion is small, a point well worth remembering when we wish to prescribe it for a stomach whose digestive capacity has been weakened   At times when whole milk disagrees we find that skimmed milk will be well handled This is possibly due to the fact that the fat which milk contains seems to have a restraining influence on the amount of gastric juice secreted, and it is also well to remember that when given by itself it is not nearly so completely absorbed as when it forms part of a mixed diet   The digestibility of the casein of cow's milk depends on whether it is precipitated in small or large clots, and we know that the latter may be avoided by the addition of lime-water, sodium bicarbonate, sodium citrate, and milk of magnesia, also hydrochloric or lactic acid, any of these substances combining with the casein tend to break up large clots, this is accomplished by interfering with the action of the rennet   Boiling milk tends to produce the same effect as just described, and, in addition, kills many bacteria   Undoubtedly casein is the great obstacle to easy digestion

Hutchison is of the opinion that just as boiling does not appreciably diminish the digestibility of milk in the stomach, so it does not to any important extent interfere with its absorption in the intestine, further, it seems to be absorbed with less expenditure of energy than any other food, and also there is reason to believe that much of the value of milk diet and milk "cures"

in many cases is due to the diminished absorption of putre-factive products from the intestine which these bring about. Needless to say there are certain cases, notably those of colitis, which absolutely reject milk, the curds acting as a decided irritant. Here we may use the various alkalies or acids as suggested, also whey, or at times the addition of farinaceous material proves efficacious

Milk is by no means a perfect food, but it is admirably fitted to supplement the deficiencies of other articles of diet. Cream, as everyone knows, contains a large percentage of fat, and is an excellent fuel Butter is, of course, a mass of fat, closely compressed, and is the most easily digested of all fatty foods It is almost completely absorbed in the intestine Koumiss and kephir are sour milks, the former being fermented mare's milk, while the latter is a fermented product of milk from the cow Buttermilk differs from cow's milk in that the percentage of fat is materially diminished, and this is probably the reason it is so much better handled in many cases than whole milk with a high fat content, and also the lactic acid bacilli are supposed to have a beneficial effect on the bacterial flora in a certain percentage of cases. It contains the casein of the milk in a finely coagulable form

Whey, as everyone knows, is the fluid which is obtained from clotted milk, and supposedly has little nutritive value Hershell and Abrahams deprecate the fact that whey has not received the attention due it, pointing out the fact that it contains the whole of the milk-sugar and the greater part of the salts and the soluble albuminoid matters of the milk It may be well to remember this in cases that are unable to digest milk curd

Cocoa and chocolate contain rather large amounts of fat, carbohydrates, and protein, and while not nearly so stimulating as tea or coffee, are more sustaining and quite nutritious They are usually prepared with milk, and this adds to their nutritive value One must not forget that they contain tannin, and are, therefore to a certain extent astringent

Cream soups manifestly are prepared from a fine purée of various vegetables such as asparagus, peas, celery, etc., the

addition of milk and cream renders them quite palatable and highly nutritious   They are extremely bland and non-irritating, and we find them splendidly received by many of the "weakling type" of stomachs

Fruit juices contain the minimum of nutrition, and it is for flavor mostly that we ingest them   We have the various acids represented according to the fruit in question—i e , grape, tartaric, lemon, citric, apple, malic—these at times chemically stimulate bowel movement and often prove valuable adjuncts when used in conjunction with other agencies

A most important factor possessed by daintily served fruit juices is the psychic effect on appetite, naturally often resulting in markedly improved digestion and nutrition   In many digestive cases our versatility in being able to handily and quickly introduce new and appetizing foods or beverages into the patient's diet will spell the difference between victory and defeat in our supervision of stubborn and prolonged dyspeptic conditions

Beef extracts, beef juices, and the various soups and broths, contrary to popular opinion, contain very little nutriment, acting more in the capacity of stimulants   The beef extracts are prepared by chopping up meat, heating under pressure with a small amount of water, and the extract is filtered and evaporated The stimulating properties are dependent upon the extractives of meat, and even this statement does not go unchallenged However, Pawlow considers them the most potent gastric excitants we possess, and claims they stimulate appetite and aid digestion   It is claimed beef extracts accelerate gastric secretion, and it is a valuable addition to other food, but in themselves must never be considered of real value from a nutritive standpoint

Beef juice cannot be classed as a real food because of the small amount of true nutriment contained therein   However, a larger amount may be used than of beef extract   The same may be said of beef-tea and the various broths

Coffee and tea are stimulants and possess practically no nutrient qualities   They contain fairly large amounts of caffein

and tannin   As regards tea, when one wishes to avoid tannin to a great extent, care should be taken to infuse for a very short length of time   A cup of tea or coffee contains about the same amount of caffein and tannin—i e, about 1½ grains of the former and slightly over 3 grains of the latter   In the great majority of digestive diseases these beverages are certainly not to be recommended

In passing, a few words may be said as to alcohol. It acts locally as an irritant, which accounts for the catarrhal condition that follows its continual use, especially when taken on an empty stomach. It causes marked secretion of gastric juice and saliva, and in moderation at times is helpful in digestive cases   Alcohol is quickly absorbed by the mucous membrane of the stomach, hence its rapid effect.

While alcohol is classed as a stimulant, this effect is transitory, as it is not favorable to producing sustained muscular effort. At times it is found advantageous to give light wines as an aid to digestion in those who are overworked or fatigued   In diabetes alcohol is at times useful as a real food—1 or 2 fluidounces may be taken daily   Wines tend to increase appetite and gastric secretion, and in moderate amounts may prove beneficial. In some wines the acid content is high, and these should not be prescribed in gouty or rheumatic conditions

We may now consider cereals as a whole   These preparations are manufactured mostly from corn, wheat, rice, oats, and barley   The chief characteristics of this type of food is the large percentage of carbohydrates they contain. Some may be slightly richer in protein and fats, as oats and rye, while corn has rather a high fat content, wheat and rye have a large amount of protein and a moderate amount of fat.

Cereals are valuable as foods, and enter largely into our dietaries in the treatment of various digestive diseases, as will be noted later   As cereals we may mention oatmeal, cream of wheat, hominy grits, cornmeal, corn flakes, etc   Macaroni, spaghetti, vermicelli, rice, and grits may also be put into this class of foods   These articles leave small residues, and are of especial value where good absorption is desired

Vegetables form another important item in our dietary assets, and are generally divided into roots, tubers, green vegetables, and fungi

The white potato is rich in starch, and contains a small amount of cellulose as compared with the various green vegetables If cooked after being peeled they lose much of their nitrogenous constituents and mineral salts, which results in a diminution of their nutritive value, therefore the cooking process should be done in their "jackets" Their digestibility as regards stomach and mouth depends on the form in which they are eaten—the purée being most easily handled, and the mealy more easily digested than the waxy (especially the new variety) In the intestine the potato is well absorbed owing to the small amount of cellulose, hence it is not of great value in sluggish intestinal conditions

There is not a great difference between the composition of sweet potatoes, yams, and white potatoes, except that the former contains about 4 to 10 per cent of sugar We may say that they are fairly digestible

The various roots, such as parsnips, salsify, carrots, turnips, beets, onions, contain a large percentage of water and varying amounts of carbohydrates, the latter much less than that found in the potato, while the fiber is greater These articles are not of great value from a nutritive standpoint, but assist greatly in balancing the diet, also their fiber materially helps in forming the ballast necessary for the proper stimulation of intestinal peristalsis On account of the cellulose contained they are often not well borne, especially in irritable conditions

We group in the green vegetable series cabbage, celery, cauliflower, asparagus, spinach, lettuce, cucumbers They, of course, offer a rich supply of organic acids and mineral salts, and, while the amount of nutriment as compared with their bulk is not great, yet it is sufficient to be of use, also the cellulose, of which there is a large percentage, is of inestimable value in stimulating the movement of the intestine, and at the same time promoting a secretion of fluid contents from its walls Constipation, with its often accompanying sluggish liver, is greatly helped by these

products The purées of these vegetables are often wonderfully helpful in various irritative conditions

The digestibility of green vegetables naturally depends upon the amount and character of the cellulose, the older ones naturally having tough fibrous tissues, while the young greens are tender and soft. In irritable conditions and very atonic states, especially the latter, which often occur in older people, the tough fibrous vegetables are not well borne

In many of these types of cases it is essential that they should be put upon a well balanced diet, and one of the requisites is vegetable articles added to the other food This is easily accomplished in the majority of cases by preparing vegetable purées, they can be made highly nutritious and palatable The vegetables are cooked (preferably by a fireless cooker for several hours or in a steamer), mashed to a pulp, then rubbed through a sieve, butter or cream added, then put in a saucepan and thoroughly heated In handling hundreds of cases we have found these purées to be most efficacious

Raw vegetables, such as tender celery, lettuce, watercress, and finely shaved cabbage made into cold slaw are often very well borne To them may be added olive oil and a small amount of salt.

The patient should always be cautioned to masticate slowly and thoroughly, and, if the advice is heeded, they will be well borne in the vast majority of cases.

Relative to purée of potato, remember there is a marked difference between the mealy part of baked potato, or that which is mashed, and properly made purée To prepare the latter, boil or bake, rub through a sieve, then beat up with cream or milk, add a small amount of butter, put in a saucepan, heat, and it is ready to serve

Dried legumes or pulses—dried peas, navy beans, lima beans, soy beans, peanuts Their chief value lies in the fact that they have a high nitrogen content in addition to carbohydrates They are quite hard to digest, not being well acted upon by the gastric juice The most satisfactory way to serve the legumes is by soaking over night, thoroughly cooking, mashing, and press-

ing through a sieve   There is an abundant amount of sulphur in peas and beans, and when they are decomposed, hydrogen sulphid is evolved, this accounting for the marked gaseous distention which often occurs after their use

The fungi, mostly represented by mushrooms and truffles, enter very little into the subject of dietetics in disease   They contain a large percentage of cellulose and are hard to digest

Fats, in the forms of butter and olive oil, are the most valuable varieties, and, on the whole, are easily assimilated. It has been reckoned that $5\frac{1}{2}$ ounces of butter can be easily absorbed with slight loss   We must always combine it with other food, as it is not well borne when administered alone or in large quantities   We often prescribe $\frac{1}{2}$ pound a day, and find it easily digested, being a most valuable adjunct in fattening rest cures

Fats and oil should be forbidden in acute digestive disorders —diarrhea, obesity, gall-stones, and gastric dilatation

Bread is characterized by a large starch content, and natur ally a certain amount of digestion takes place in the mouth. The more thoroughly bread is masticated, the more complete will the conversion of starch be   Toast, crisp crackers, and biscuits are much easier to pulverize than bread, and because of the thorough and continued chewing necessary a large amount of saliva is called forth, thus making another potent factor in the process   One must not forget the reflex and psychic production of gastric juice from this procedure   Fresh bread is hard to chew and does not allow of thorough absorption of the saliva, further, it is resistant to the action of gastric juice   In the intestine absorption of white bread is marked by its thorough ness, however, the proteins are proportionately not nearly so well absorbed as those of meats   Bread is not unlike milk in one attribute—it apparently is better absorbed when combined with other foods   Brown and whole wheat breads contain more bran than the white, and because of the increased amount of cellulose contained are not as completely absorbed in the in testine

Bread is certainly one of our most nutritious foods   One

must remember that three fifths of it consists of solid nutriment and two-fifths water—a ratio approached by but few articles of diet.

As with milk, so it is with bread—a splendid nutritious food, but not complete—therefore the best results are obtained by supplementing it with other substances

Meat is composed of muscle-fibers, connective tissue, fat—the comparative amounts of each differing in the species of animal, poultry or fish, and the various cuts   A large amount of fat may serve to diminish the digestibility of the meat.

From what has been said it is obvious that protein and fat are the chief constituents of the above foods, but one must remember that water enters largely into the composition of meat. It is of interest to note that cooking diminishes the amount of water in meat, resulting in an increase of its nutritive value, but at the same time tends to lessen the digestibility, hence it is best to serve underdone meat to weak stomachs As to the comparative digestibility of the various meats there is a difference of opinion, but veal and pork are probably the most indigestible, however, one must never lose sight of idiosyncrasies possessed by various people   The breast of chicken and game is especially well digested, and we know that meat as a whole is quite thoroughly absorbed in the intestine, leaving little residue   It is our source from which building material is obtained for the body, also one of its attributes is that it has a stimulating effect, and Hutchison is of the opinion that the feeling of well being which follows a meat meal may be put down to this cause   The amount of fat contained in various meats is of fundamental importance regarding their nutritive value Liver, kidney, and sweetbreads have a high nucleoprotein content, and are often eliminated from the diet, especially in the case of those of a gouty diathesis   Sweetbreads, however, are easily digested

As regards fish, there is nothing of especial moment to discuss   Like meat, the chief constituents are protein and fat, the former, of course, dominating to a great extent—salmon, salmon trout, mackerel, turbot, and herring contain the largest

amounts of the latter   Fish contains more gelatin and fewer extractives than meat. Their absorption is quite complete, and they are very nutritive, the degree of the latter depending on the amount of fat   Of oysters, there is not much to say They contain a small amount of protein, fat, and carbohydrate, consequently are not very nutritious, but easily digested and absorbed quite completely

The chief constituents of cheese are casein and fat Examples of the hard variety are Edam, Cheddar, Roquefort, soft, Stilton, cream, Camembert, Brie, and Neufchatel The stomach is unable to digest the cheese, but after its entrance into the intestine not much difficulty is encountered—it is thoroughly absorbed The reason for the difficulty of digestion lies in the fact that cheese contains a large percentage of fat, and this prevents the gastric juice from gaining access to the casein A given quantity of cheese yields a much greater number of calories than the same amount of meat Our experience is that the soft cream cheese is the most digestible of all varieties

Eggs consist of the white and yolk, the latter being its most nourishing portion They contain rather good amounts of protein and fats, practically no carbohydrates Lime, iron, and phosphoric acid are the most important mineral constituents Eggs are quite easily handled by the stomach, the soft boiled leaving it in the shortest time If a hard-boiled egg is finely divided and thoroughly masticated it is disposed of as well as the soft boiled We find at intervals patients who have a true idiosyncrasy toward eggs, and many times they cannot be taken They are easily digested in the intestine and leave little residue Their nutritive value is due almost entirely to protein and fat.

It cannot be said of fruits that they are of great nutritive value However, the greater part of nourishment which they do contain is present as the carbohydrate group, and a large percentage of this is in the form of sugar, usually levulose, although apples, apricots, and pineapples also have in them cane-sugar Cellulose is present in all fruits, but necessarily is rendered quite soft and more digestible by the cooking process

One must remember that the mineral constituents—*i e*, potash combined with tartaric, citric, and malic acids—at the end of the metabolic process render the blood more alkaline and the urine less acid   Fruit which has not thoroughly ripened, thus having a greater amount of hard cellulose with excess of acids, is not well digested, and the latter often prove irritating to the digestive tract. If the ripening process has been allowed to go to maturity, the more moderate amounts of cellulose and acids often act as mild stimulants, mechanically and chemically, upon the intestinal wall, often greatly assisting a sluggish bowel   (It may be well to state at this time that here, as in other discussions of the various articles of diet, for the precise percentages of protein, starch, fats, etc., the reader is referred to standard text books)

Nuts are of high nutritive value because of their richness in protein, fat, and carbohydrate, but are quite indigestible, due to the high fat and cellulose content.   While thorough mastication will overcome this to a certain extent, it is more satisfactory and effectual to have them artificially ground   The various butters and preparations made from nuts are highly nutritious   It is interesting to note that they closely resemble meat in their general make up, and are even a more concentrated food than cheese

Sugar is a most important article of diet, and some valuable deductions may be succintly put by quoting from Hutchison

"Sugars in the stomach tend to undergo fermentation

"I   Alcoholic, resulting in the production of alcohol and acetic acid

"II   Butyric, with the formation of butyric acid

"III   Lactic, the product being lactic acid

"Practical deductions

"I   In dyspepsia the absorption of carbohydrates is delayed, and therefore all sugars tend to ferment.

"II   In dyspepsia with lactic acid formation one should avoid dextrose, levulose, and invert sugar, and use cane-sugar, maltose, and lactose in moderate amount.

"III   In butyric fermentation lactose should be preferred

"IV In alcoholic and acetic fermentation one should forbid invert sugar and levulose, and give lactose

"It will be observed that of all sugars, lactose is least liable to fermentation   This is another point in favor of the value of a milk diet in stomach complaints "

However, from practical experience, we see that if sugar is taken in moderation with other foods it is, in the great majority of cases, well handled   In contradistinction to meat, sugar is probably the chief source of muscular energy

Spices and condiments probably act reflexly through the organs of taste, and also may have some direct action upon the stomach itself in calling forth a secretion of gastric juice—they act as irritants, and are contraindicated in ulcerative or irritative lesions of all kinds   Mustard, pepper, vinegar, nutmeg, allspice, cinnamon, and cloves may be considered examples of spices and condiments

Of desserts, we may mention gelatin (in most cases with cream added on account of nutrition), custards (boiled or baked), blanc mange, jellies, tapioca, Spanish cream, ice-cream, etc

With the exception of gelatin the above-mentioned articles markedly resemble one another in composition   Gelatin is considered a protein sparer, and the calf's foot jelly as purchased contains about 4 3 per cent of protein and 17 per cent of carbohydrates   It is easily digested and has the capacity of fixing a large amount of acid—hence its efficacy in hyperacid conditions The other preparations are made with sugar, butter, eggs, milk, and salt, therefore their intelligent application in various conditions would depend on our knowledge of the different percentages of the individual ingredients

Recapitulating for a moment, it will be noted that we have discussed the various fundamentals with which we should be familiar—the types of food and their individual characteristics We are now prepared to apply our knoweldge in a practical manner to the diseased condition of the digestive tract   It would manifestly be impractical to discuss separately the many diseased conditions of each digestive organ therefore it seems

best to deal with the subject in a general but at the same time detailed manner

We shall first deal with ulcerative lesions, and at this moment one must have in mind the underlying pathology and anatomy of the part in question

In beginning the diet in these cases, bland, non irritating, and, as far as possible, nourishing liquids should be given, so that the minimum amount of endeavor is brought forth from the affected organ   We now refer to the list of such articles, and find milk and egg albumen stand at the head   In starting liquid diets remember to give them in small amounts (1 to 3 ounces) frequently repeated (one to two hours), depending upon the patient's ability to handle them   Here let it be pointed out that the ironclad following of text-books in giving ulcer cures—*i e*, adhering to amount, hour of administration, number of days such and such an article is kept up, etc.—is most pernicious, and a little later we will discuss how each practitioner can intelligently and correctly judge for himself in the vast majority of cases just when to increase the dietary   If milk is not well borne, then remember the advice given regarding the addition of various alkalies, also the use of skimmed or parboiled milk, whey, albumen, buttermilk, malted milk (fruit juices are often well tolerated)   One will note that cream soups, cocoa, and chocolate are included in the bland, non irritating liquids.   However, it will be well to administer these later when the stomach is handling other food in a satisfactory manner, and at a time when we are especially desirous of increasing weight, for in the weakened state of digestion we often find fats not well tolerated

When we wish to increase the amount and change the consistency of nourishment slowly, we simply advance to the gruels and mushy foods—watery gruels of strained oatmeal, farina, cream of wheat, hominy grits, cornmeal, vermicelli, rice, purée of potato, spinach, asparagus, peas, and cauliflower   These watery carbohydrates call forth the smallest amount of gastric juice   therefore causing the slightest efforts to be brought into play by the stomach   Smithies very aptly suggests flavoring

the above with coffee, chocolate, vanilla, and caramel, also adding small quantities of arrowroot or cornstarch in order to produce a thin emulsion

If the digestive apparatus is not burdened by the above class of nutriment, then access may be had to those of a degree nearer solids—the soft cereals in what might be termed their native state—oatmeal (best strained), farina, cornmeal mush, hominy grits, cream of wheat, etc

Eggs in very soft states, as boiled, scrambled, poached, raw, or well beaten in milk

Small amounts of cream soups may be tried

Purée of vegetables, as mentioned above

Purées of fruits, fruit juices

Toast (stale, sliced thin, and thoroughly dried out in a slow oven), crisp crackers

Cream cheese

Butter

Beverages may be selected from those mentioned above

Soft desserts

If we now again wish to advance our line of diet, the following general dietary may be applied (from lists noted above)

Cereals, eggs (all styles except fried), cream soups, potatoes (baked or well mashed), rice, macaroni, spaghetti, asparagus, spinach, tender string beans, Brussels sprouts, peas and beans, cauliflower, onions, creamed carrots, turnips, beet greens, baked squash, rhubarb, lettuce   (It is safer to continue the fibrous vegetables in purée form for some time)   Toast crackers, crisp upper layer of corn bread   Milk, buttermilk, malted milk, cocoa, chocolate   Stewed fruits and their juices, soft part of baked apple, apple float, prune whip   Cream cheese, butter   Light desserts, including well-made rice or bread pudding   Raw fruit, such as apples, peaches, and pears, are usually not well borne   Meats should be the last articles of diet to be allowed—tender breast of fowl, lamb, rare hamburger steak or beef, fish (boiled or baked), soft part of oysters   None of those mentioned should ever be fried, and should not be allowed under three to six months

An admonition was made as to avoiding hard and set rules for increasing, decreasing, or applying new articles of diet. How may everyone become efficient in this regard? There are four points (1) Subjective symptoms of patient—nausea, pain, discomfort, etc., if these are markedly ameliorated, it is time to consider increase in diet (2) Objective—tender points, muscle spasm, pain on pressure, vomiting, melena, and general appearance, an improvement in these likewise should be of value in pointing the way to progressive measures. (3) Microscope—stool examinations to determine if various food stuffs are being digested, also if mastication has been complete. (We can often in this manner keep a good check on one who slights mastication, bolts food, and then wonders why he does not improve) (4) Stool—investigation for occult blood, note intensity of reaction, and then watch for diminution and final disappearance A careful study and résumé after close analysis of the information obtained by the above methods will enable us to intelligently know just about the time to make the necessary changes

The above principles of treatment may be applied to ulcerations of esophagus, stomach, intestines, in spastic states of these organs from reflex conditions, such as pylorospasm from chronic appendicitis, gall-bladder, duodenal ulcer, etc.

Let us see how simple it is to apply dietetic treatment to acute inflammatory conditions of the digestive tract We must always consider first the pathology, and from this we will learn whether bland, non irritating substances and those leaving little or no residue are indicated, or, on the other hand, foods which from mechanic, chemic, and thermic stimulatory standpoints are to be used We have learned that all tissues showing acute inflammatory reactions should not be stimulated, but rested, therefore after the preliminary evacuation of gastric and intestinal contents by the various methods, followed by a period of starvation, we apply liquids of a bland, non irritating variety, it is not essential that they should be extremely nourishing in the acute cases, therefore we refer to our list of non irritating fluids, probably the safest one to try is egg albumen, and this may be given in fruit juices, if well borne, gradually en-

large the number and amount of the various liquids   Attention should be called to two points   One is that at times in gastric and intestinal acute upsets milk is not well borne, therefore, if given at all, it should be well diluted, skimmed, parboiled, or alkalies added   The second point, although the broths are classed as stimulating, they need not be irritating, they leave no residue, and if well diluted often act splendidly   From these we graduate to watery carbohydrates, soft purées and cereals, soft eggs, custards, toast, and on through the list, until we finally enter again upon a good substantial diet, and again, at the expense of being monotonous, add meat as the last article. A practical point may be enumerated—when you do give meat, start on scraped (not chopped) beef, for here we have only the tender muscles without connective tissue   Make this into cakes and slightly broil, succeed this by breast of fowl, and later meats in rare state passed through a food chopper, before returning to meat in its natural form   The latter would be a splendid procedure to follow with the more mature and high cellulose content vegetables

The pathologic conditions which may be successfully handled by the above methods are acute inflammations of esophagus, stomach, small and large intestines from the various etiologic factors

As a sequel or result of the above processes we meet at various times the chronic inflammatory states, which may be of benign, malignant, leutic, or tubercular origin   Almost needless to say the pathology here met with is quite different from that just discussed   While the inflammation is chronic, yet we must bear in mind it is not restored to normal by keeping up a continued irritation, therefore we should apply food which, while non-irritating, yet, because of various properties, acts as a mild stimulant, coaxing, as it were, a diseased organ back to the normal   Here again we avoid heavy articles which may cause mechanic, chemic, or thermic irritation, and in lieu of these we transform these very foods into benign, moderately stimulating and helpful, health-restoring mediums   You ask how? We merely refer you to soft cereals—eggs, various purées (vegetable)

—not forgetting to especially call your attention to the fruits as purées—*i e*, apple float, prune whip, and the like, toast— hard? Yes, but earlier we have pointed out how, if care and attention is directed to thorough and painstaking mastication, a soft mass thoroughly impregnated with saliva is produced, calling forth not only splendid salivary secretion, but, in addition, a reflex gastric flow, thus preparing the stomach to receive the soft minutely comminuted food This is a point well worth emphasizing Now graduate your diet up through the various grades, and you will have solved the problem of chronic inflammations

Just a word as to mucomembranous colitis In this condition the spasticity of the gut with some degree of inflammation are the causative factors producing quite often, among other symptoms, obstinate constipation. Our object is to give mild stimulating food in finely divided states and nutrient in effect— soft cereals, carefully prepared purées of vegetables, and fruits (apple, pear, plum, apricot, prunes), spaghetti, macaroni, vermicelli, well-boiled rice with the soft desserts, milk puddings of tapioca sago, rice, cream soups, toast, crisp crackers make an ideally suitable menu Later chicken and beef, prepared as described earlier, may be cautiously added Use the microscope, and if only a few, well rounded, non-striated muscle-fibers are noted, then we may forge ahead with some temerity, but if they are sharp on ends, many in number, and well striated, we know digestion is incomplete, and it is time to consider a retrenchment In the early treatment beef extracts and juices should be withheld also, as pointed out above. The safest procedure is to start with bland, well-divided, non irritating, farinaceous material, cautiously working up to the vegetables, etc

Some authors use a diet diametrically opposed to the above advice, and give coarse green vegetables, coarse fruits, and meat This may be followed, but our personal feeling is that the soft non irritating form of food forms a more natural line of treatment

Regarding diet in various stenoses—esophagus, stomach,

intestine—one finds here an easy and simple discussion The spastic variety is handled in identically the same manner as the first and second stages of ulcer, i e , bland liquids, followed by finely divided, farinaceous foods, then purées Just a word as to change from purées to solids—go very, very slowly and exert the utmost caution relative to meat even in the finely divided state

It may not be amiss to state, what is known to every medical man, organic stenosis is fundamentally surgical in the vast majority of cases, however, if we wish to treat it dietetically, our opinion is that the soft, moist purées are better borne and more effectually dealt with by the stomach than heavy foods or large amounts of liquids, therefore after the stomach has been thoroughly lavaged, small, frequently repeated meals consisting of the foods just mentioned are far preferable to large meals at long intervals Excesses of farinaceous and fat foods should be avoided on account of fermentation The character of lesion, be it benign, malignant, tubercular, or luetic, has no bearing on the application of the above principles

Acute appendicitis after the starvation period is dieted according to the methods enunciated in acute inflammatory ailments

Chronic appendicitis often results in reflex pylorospasm, ulcer, and spastic constipation, therefore reference to these states will supply all necessary knowledge concerning this pathologic lesion

Hyperchylia gastrica and hyperchlorhydria are symptoms and not distinct disease entities They result from intrinsic and extrinsic lesions, such as gastric ulcer, inflammations, duodenal ulcer, chronic appendicitis, gall-bladder involvement, etc When the diagnosis has been made, treat the offending organ Also it will be well to caution that it is best to restrict the use of bread, potatoes, sugars, and all sweet and sour articles of diet in these ailments

Two conditions often met with which interest us clinically and dietetically are protein putrefaction and carbohydrate fermentation In the former eliminate protein of all character

and give the green vegetable and fruit purées, then farinaceous purées, etc gradually working up to general dietary, including meats, for here we usually have a marked derangement of normal intestinal capacity, add very minute (finely divided in food chopper) amounts of tender breast of fowl, lamb, etc., intensely scanning stools with microscope and closely watching reaction with litmus, also noting color and general consistency   In the latter condition (carbohydrate fermentation) all carbohydrates are withdrawn, and a protein fat régime inaugurated—finely divided meats, fish, soft part of oysters, meat broths, butter, eggs. There is such a small amount of carbohydrates in well-cooked and puréed green vegetables that the latter are usually allowed—i e , asparagus, spinach, cauliflower, carrots, peas, squash, celery, beet tops, etc. When these are well borne, experiments may be tried with very small amounts of white potato, bread, rice, etc.

In achylia gastrica again we think of the pathology of the part—attenuated, atrophic glands in many cases, absence of digestive juices, gaping pylorus, slight reflex stimulation of pancreatic and liver secretions, hence the food as received in the stomach is passed on to the intestine   Manifestly then the diet should be taken in such a state as to throw the slightest burden in every manner upon the stomach and intestine. This is accomplished by bringing into use soft, farinaceous foods, cereals eggs, purées of vegetables and fruit, toast, crackers, butter, cream cheese, light desserts   If meat, fowl, or fish are allowed, it should be given in scraped or finely divided form   Milk (variously prepared) and buttermilk are usually well borne, and cocoa, chocolate, weak tea, or coffee may be tried

Pancreas The conditions in the intestine in disease of this organ are very similar to those found in achylia, and if the power of all enzymes are diminished or absent, it means there will be a great decrease in the digestive action of the intestinal juices. The only way then—from a dietetic standpoint—to deal with such a weakened digestion is to make its duties less arduous This is accomplished by following out the same rules made use

of in achylia, working back, of course, to approximately a normal diet as soon as the functions of the organ will permit.

Liver   The same diet may be applied here as in the chronic inflammatory conditions of the stomach and intestines, as ofttimes both are due to the same etiologic factor, food should be well divided and non-irritating, especial care being taken to avoid fats and rich food, also sugars and carbohydrates

As regards gall-stones, practically all authors are agreed that small, frequently repeated meals are preferable to large and infrequent ones, as it is generally agreed that the discharge of chyme from the stomach greatly increases the flow of bile into the duodenum, due to a reflex mechanism dominated by the law of contrary innervation

Large amounts of water should be insisted upon

Constipation   We generally have one or two types to deal with   (1) Atonic, (2) spastic   In the former a stimulating diet, such as the following, is to be recommended

Oatmeal (2 or more heaping teaspoonfuls of bran), Petti johns (25 per cent bran), shredded wheat (cream may be added to cereals), various fruits (raw or stewed), apples, pears, dates, figs, etc , also fruit juices, green vegetables, spinach, celery, lettuce, cabbage, Brussels sprouts etc , whole wheat, bran, graham breads, honey, marmalade, molasses, buttermilk, cider   Small amount, if any, of meat   Avoid tea, coffee, red wines, cocoa, chocolate

It is often found advantageous to take one or two glasses of water (hot or cold) every morning on an empty stomach in an endeavor to inaugurate peristalsis

The spastic type is treated by using practically the same articles of diet, except they are given in the finely divided state One can generally follow the means mapped out in mucous colitis

In conclusion it may be well to discuss a few odds and ends

Very often we are asked to outline for a patient who has retable containing suggestions for a well-balanced diet   The covered from one or more of the previously discussed ailments a following may serve this purpose

Breakfast   Fruit—orange, grape-fruit (one-half)
           Saucer cereal and cream, or soft eggs.
           Roll or slice of toast—buttered.
           Cup Kaffe Hag Postum, or milk flavored with coffee.
           Sugar (not over one lump)

Lunch.   Cup of clear broth.
           Small baked potato
           Helping green vegetable
           Saucer stewed fruit.
           Roll, Graham bran or whole wheat muffin.
           Cup weak tea.

Dinner   Cup cream soup.
           Chicken fish lamb chop, beef
           Baked potato rice, macaroni (one choice)
           Lettuce salad
           Bread as above—Uneeda or cream lunch cracker
           Butter
           Light dessert as per suggestions above, with small amount of
              American or cream cheese.
           After dinner cup Kaffe Hag or some coffee substitute.

Generally speaking, articles to be avoided are pepper, mustard, vinegar, condiments of all kinds, rich pastries, pickles, gravies Abstain from excesses of bread and potatoes, sugar, and sweet things As to alcohol, the safest course is to eliminate it entirely

If with the above we wish to suggest intermediate feedings, the following may be brought into play Cup of broth or cream soup with several buttered crackers, cup custard, blanc mange and the like, milk, buttermilk, milk-shake with egg, or any of these combinations served in an appetizing manner They may be taken between meals and at bedtime

Always remember that certain people have marked idiosyncrasies regarding particular food-stuffs, therefore it is wise to bear this point in mind

In chronic cases do not keep upon soft, sloppy food longer than absolutely necessary Our experience has been that if food is repugnant to patients it is much better to substitute other varieties even though in some respects it is contraindicated The psychic factor undoubtedly plays a major rôle

In nervous, dyspeptic, or functional conditions, treat symptomatically, and as soon as possible put upon a good general dietary, such as that just suggested These cases should not be pampered dietetically

CLINIC OF DR. ELMER B FREEMAN

JOHNS HOPKINS HOSPITAL (OUT PATIENT DEPARTMENT)

ESOPHAGOSCOPY AS AN AID IN THE DIAGNOSIS AND TREATMENT OF ESOPHAGEAL DISEASE

Introduction.—In presenting this Clinic on Esophagoscopy I desire to very briefly review the early literature on the subject, to mention the indications for and the contraindications to esophagoscopy, to describe the method of examination and to discuss esophagoscopy as an aid in the diagnosis and treatment of esophageal disease

Johnston, Janeway, Yankauer, Mosher, Stillman, Chevalier Jackson, and others

Indications —The indications for esophagoscopy are the presence of a foreign body in the esophagus and all other conditions in which there are discomfort, pain, or difficulty in swallowing

Contraindications —The contraindications are aortic aneurysm, cardiac disease with hyperthrophy, arteriosclerosis with hypertension, advanced pulmonary tuberculosis, cirrhosis of the liver and curvature of the spine (in the cervical or dorsal region), but these are not contraindications if the esophagoscopy is being done for the removal of a foreign body

Method —Before an esophagoscopic examination the patient should have a preliminary physical examination, and frequently an x-ray study to exclude contraindications

Children under six years of age very frequently can be examined without the use of an anesthetic   The child is wrapped in a sheet, placed on the table in dorsal position, and firmly held by two assistants   If for any reason an anesthetic is necessary, a general anesthetic should be used and the preference given to ether   Local anesthetics are very dangerous in children, and the deaths which have occurred under general anesthesia have been when chloroform was used

In adults the examination can always be made by using a local anesthetic except in cases of the removal of very large foreign bodies where it is necessary to give ether to thoroughly relax the patient

My routine has been as follows   The patient is seated on a low stool, the head held by an assistant, in almost complete extension, and three or four applications of 10 per cent solution of cocain (on cotton applicator) are made to the laryngopharynx, then the esophageal speculum is introduced, and, if necessary, two or three applications of cocain are made to the right pyriform sinus and the upper end of the esophagus   Before the esophagoscope is passed the esophageal speculum should be introduced and a careful inspection made of the pyriform sinuses and the upper end of the esophagus   By doing this we frequently find

diseased conditions which might otherwise be overlooked The esophageal speculum is now passed through the right pyriform sinus and the larynx is gently brought forward, this brings into view the slit like opening of the esophagus The right pyriform sinus is selected because the esophagus in its downward course passes slightly from right to left, making it very much easier to enter the esophagus through the right pyriform sinus The esophagoscope should be passed without the obturator, as this gives a better opportunity to study the esophagus When the instrument is introduced to the cricoid region it meets with more or less definite resistance This is caused by the contraction of the inferior constrictor muscle of the pharynx, this resistance is quickly overcome if a slight degree of pressure is used After the cricoid region is passed in a normal esophagus there is no difficulty in passing the tube down to the cardia. There are four regions in which a normal esophagus shows narrowing of the lumen first, cricoid, second, crossing of the arch of the aorta, third, crossing of the left bronchus, fourth, at the diaphragm, these are respectively 16, 23, 27, and 37 cm from the incisor teeth. The cervical portion of the esophagus is a collapsible tube, the dorsal portion remains open, showing a slight dilatation during inspiration and a slight contraction during expiration The mucous membrane is soft, smooth, and has a pale pink tinge which changes to a reddish hue at the cardia

The esophagus is to be studied during the withdrawal of the tube as well as during the introduction, for in some cases a better view is obtained while the instrument is being withdrawn. The conditions in which esophagoscopy aids in the diagnosis are carcinoma, cicatricial, spasmodic, and pressure stenosis, ulceration, and diverticulum

Carcinoma —In malignancy the esophageal picture varies with the duration of the disease Unfortunately, we do not see most of these cases until the disease is quite far advanced, for the patient does not seek relief until obstructive symptoms have occurred, and these are only found late in the disease The upper portion of the esophagus should be examined with the esophageal speculum and the examination completed with the

esophagoscope In my own experience I have seen more cases in the upper than in the lower and middle third of the esophagus. In making these examinations one is impressed with the inelasticity of the esophagus, which gives a sensation of firmness to the esophageal wall, also with the small amount of dilatation above the growth The inelasticity of the esophageal wall is due to the cancerous infiltration, and the small amount of dilatation is due both to the infiltration of the esophageal wall and to the obstruction occurring late in the disease In cases where the growth is submucosal it is quite easy to pass the diseased area unnoticed, however, in most of these cases there is a bulging of the esophageal wall with a sensation of hardness or firmness when the tube is passed Jackson calls attention to white patches in the mucous membrane which look precisely as though the mucous membrane had been burned with silver nitrate. He believes that these patches may be the manifestation of early malignancy, and claims that they cannot be diagnosed in the endoscopic picture from luetic lesions In the more advanced cases the growth has a polypoid appearance which may or may not have undergone ulceration If the growth is ulcerated the border of the ulcer is irregular and the surface bleeds very easily While making the examination it is very easy to remove a specimen with a cutting forceps for microscopic study, and this should always be done if there is any doubt in regard to diagnosis

Cicatricial Stenosis —Most of these cases are the result of the healing of ulcers produced by swallowing corrosive poisons, some, however, are caused by the healing of ulcers associated with tuberculosis, lues, acute infectious diseases, and after the removal of foreign bodies In my own experience in the corrosive cases the stenosis has occurred in the middle and lower third of the esophagus, in tuberculosis and lues, in the upper third, cases associated with acute infectious disease I have not seen, but Jackson and others have reported quite a number Jackson especially calls attention in the typhoid cases to the stenosis occurring in the cricoid region It is only found in the very toxic cases, and is thought to be due to the healing of an

ulcer produced by the cricoid pressing the esophagus back against the spine   Cases that occur after the removal of foreign bodies are most frequently found in the upper third of the esophagus because most foreign bodies lodge in that location, but recently I have seen one case in which Dr Johnston of Baltimore had removed a foreign body from the middle third of the esophagus two years previous to my examination, this patient complained of marked difficulty in swallowing   The esophageal examination showed a slight degree of stenosis   The esophagoscopic picture as presented through the esophagoscope varies with the degree of the stenosis and the period of time that it has existed In cases of moderate-degree stenosis the scar tissue is not extensive and there is very little dilatation above the stricture, but the mucous membrane shows some evidence of chronic inflammation.

In cases in which there is almost complete stenosis the endoscopic picture is very different, the scar tissue is quite extensive, and may almost completely encircle the esophagus, there is definite dilatation above the stricture, which gives the esophagus a characteristic funnel shaped appearance, and in the dilated portion there are chronic inflammatory changes of the mucous membrane with superficial ulceration   In cases of complete stenosis the scar tissue is so extensive it completely excludes the esophagus

Spasmodic stenosis of the esophagus probably occurs more frequently than we have thought   It is sometimes due to simple ulceration of the esophagus, but usually it is reflex, and as such may be associated with a great many conditions   It is the impression of the clinic that gastro-intestinal lesions, especially gastric and duodenal ulcers, are potent factors in its production Underlying all of these factors is a definite neurotic state of the patient

Spasmodic stenosis may occur at any level, but it is especially prone to occur in the cricoid region and at the level of the diaphragm

In cases occurring in the cricoid region one is impressed with the increased resistance to the passage of the esophagoscope,

there is very little dilatation, the mucous membrane is perfectly normal in appearance, and if firm pressure is exerted the spasm relaxes and the tube passes on through the esophagus

The most interesting cases are the cases occurring at the level of the diaphragm These cases have been spoken of in the literature under the head of "cardiospasm," but this term really should not be used, as the condition is not one of spasm of the cardia, but one where the spasm occurs some distance above the cardia at the level of the diaphragm Jackson uses the term "hiatal esophagismus" in describing this condition. The endoscopic picture depends mostly upon the duration of the condition Most of the cases studied are those in which the condition has existed for a number of years There is very marked dilatation of the esophagus above the seat of the trouble, the mucous membrane shows definite evidence of chronic inflammation and may show some areas of superficial ulceration The dilatation is so great in some of the cases that it is necessary to wash out the esophagus before a satisfactory examination can be made I recall one case in which more than a quart of thick mucous fluid was removed In these cases if gentle but firm pressure is made the spasm relaxes and the esophagoscope passes into the stomach

Ulceration —Esophagoscopy is the only reliable means we have of diagnosing an ulcer in the esophagus, but to determine that it is a simple ulcer requires the exclusion of tuberculosis, lues, and malignant disease Simple ulcer is usually associated with cicatricial or spastic stenosis If stenosis is not present, we must think of the ulcer as probably being tuberculous, luetic, or malignant The tuberculous ulcer is not associated with inflammatory changes in the mucous membrane, is not elevated, and does not bleed easily The luetic ulcers are frequently associated with a great deal of scar tissue, with marked evidence of inflammation, with an elevated irregular border, and with very little bleeding when sponged The malignant ulcers are characterized by being very red and angry looking, the surface is raised and irregular, bleeds very easily, and the base has a

very definite sense of resistance. Tuberculin and Wassermann tests should be done to aid in the differential diagnosis.

Diverticulum.—Esophagoscopy aids very much in the diagnosis of diverticulum, but the examination should always be preceded by a careful x ray study so as to get a correct idea of the size and location of the pouch. Most of the cases occur high up, and the hernial sac is found to come off from the esophagus just below the cricoid cartilage, however, it may occur lower down, and is then due to adhesions from some of the surrounding organs to the esophagus, these causing traction and pouch like dilatation. In doing esophagoscopy in these cases the tube apparently enters a blind pouch, but if careful examination of the anterior wall of the pouch is made a slit-like opening will be found which is the entrance to the lower portion of the esophagus. The finding of this opening makes the diagnosis complete and differentiates the condition from cicatricial stenosis with dilatation.

Pressure Stenosis.—In this condition the stenosis is usually due to an enlarged thyroid, mediastinal disease, aortic aneurysm, or enlarged heart. Each of these conditions is a contraindication to esophagoscopy, and the examination should not be resorted to unless it is for the removal of a foreign body.

Foreign Bodies.—In suspected cases of foreign body in the esophagus one should first have an x ray study, and if by this method a foreign body is found, its size, shape, and location is to be carefully noted. If the foreign body is small and not very dense, it may not be located by the x ray. In these cases it is necessary to search for the intruder endoscopically. If the foreign body is very large, it will be necessary to give a general anesthetic for extraction, as the relaxation produced by general anesthesia makes it possible to remove it with less traumatic injury to the esophagus and danger to the patient. As mentioned before, ether is the only anesthetic which can be used with safety. All of the mechanical problems connected with the removal should be worked out and necessary instruments at hand before an attempt at removal is made, as an unsuccessful attempt makes subsequent efforts more difficult. About

90 per cent of foreign bodies that lodge in the esophagus are found above the cricoid cartilage, and these can usually be removed by the aid of the esophageal speculum Those located in the middle and lower third of the esophagus require very careful endoscopic study and manipulation If the foreign body has been in the esophagus a number of days the difficulty of extraction is increased by inflammatory swelling and edema, therefore the endoscopist should proceed very carefully so as not to override the foreign body and pass it unnoticed When located, the foreign body should be studied and the best method of removal decided upon, and then the instrument best adapted to its extraction should be used The after-care of the patient consists in giving of nothing but ice-cold liquids, or ice-cream for forty-eight hours, and then a bland, non-irritating diet until all the symptoms have subsided—no drugs are indicated If the foreign body has caused ulceration the case should be watched for symptoms of stenosis which may occur when healing takes place

TREATMENT

Spasmodic Stenosis —In treatment of spasmodic stenosis one has to remove if possible the etiologic factors, for example, if the spasm is associated with gastric or duodenal ulcer, this condition must be treated To control the spasm there is no drug that compares with belladonna My custom has been to give the belladonna to the physiologic tolerance, sometimes giving as much as 40 to 50 drops three times a day In all the cases of esophageal spasm that I have treated I have not found one that could not tolerate very large doses I have also given these patients small doses of mineral oil three times a day to allay the irritation in the mucous membrane After the patient is well under the influence of belladonna (usually by the tenth to fourteenth day) mechanical dilatation is begun For the cases occurring in the upper third I have simply passed the large esophagoscope, this has relieved most of the cases after the first passage In a few it has been necessary to repeat the treatment The cases which have occurred at the level of the diaphragm have been treated with the Plummer dilator either

with air or water pressure In cases where there was difficulty in getting the dilator in place the olive tip has been threaded over a thread swallowed the day before, and with the thread as a guide there has been no difficulty in placing the dilator and dilating the stricture This treatment is repeated twice a week, and later, when the patient has improved once a week The other methods are mechanical divulsion from above and gastrostomy with forcible dilatation from below The choice between using the mechanical divulsor or dilating with water pressure is a personal one, as both methods give good results but I do not see anything to be gained in doing a gastrostomy with forcible dilatation from below when these cases can be dilated from above without operative treatment

These patients should be kept on small quantities of liquid food every two hours while dilatations are being made By feeding in this manner all pressure is removed from the esophagus After the patient has been relieved clinically, soft food may be added—no coarse or irritating foods should be given until a few months after treatment has been discontinued In cases with marked dilatation the esophagus should be emptied of all food before retiring, as this removes all irritation and relieves some of the annoying symptoms While treating these cases we have made frequent fluoroscopic examinations, and while the patient has been relieved clinically the esophageal dilatation has persisted

Cicatricial Stenosis —In this condition there is an associated spasmodic condition as well as the organic lesion which calls for treatment The associated spasm is treated by giving belladonna and mineral oil The belladonna should be given to the point of physiologic tolerance The management of the organic stenosis depends on the extent to which the lumen of the esophagus is narrowed If the esophagoscopic examination shows that the stenosis is of moderate degree, that the mucous membrane above the stricture is not inflamed or ulcerated the treatment consists of simply dilating with a bougie or a silk woven sound In these cases the silk woven sound is to be preferred as it is not necessary to dilate through the esoph

agoscope In cases of high-grade stenosis, where the patient
is starving and the tissue suffering for want of fluid, the first
thing to do is a gastrostomy, and by feeding in this manner the
esophagus is given absolute rest and at the same time the
patient is nourished It is absolutely impossible to treat the
esophageal condition unless the esophagus is given complete
rest When the patient's condition improves an x-ray study is
made to locate the level of the stricture and to note the amount
of dilatation above the stenosis, an esophagoscopic examination
is also made to note the character of the stenosis and the amount
of ulceration and inflammation above the obstruction No di
latation should be attempted while there is ulceration and in
flammation present It has been my rule to give nothing by
mouth except belladonna and mineral oil until after the esopha
gus has been dilated a number of times In the beginning the
olive-tipped bougie is passed through the esophagus and later
on the silk woven bougie is passed without the 'scope The
gastrostomy opening should not be closed until the esophagus
can be dilated to normal size When mouth feeding is resumed
the bland, non-irritating liquids are given, and if these are
well tolerated the diet should be increased, avoiding, however,
for a long time coarse vegetables and uncooked fruits In cases
where the stenosis is complete a gastrostomy must be done to
prevent starvation, and an attempt should be made to relieve
the stenosis by operation

Ulceration —All patients with ulceration of the esophagus
should be placed on a bland, non-irritating diet, and frequently
it is necessary to allow nothing but liquids If the ulceration is
associated with tuberculosis or malignancy the treatment is
merely palliative If due to lues, it responds to antiluetic treat-
ment If it is a simple ulcer it should be treated by the applica
tion of some of the silver salts—argyrol in a 20 to 25 per cent
solution being applied endoscopically every few days—usually
three to four applications will suffice

Carcinoma —Unfortunately, the only treatment is pallia-
tive When obstruction occurs, some advocate intubation of
the esophagus, others favor dilating with sounds, but both of

these methods mechanically irritate the growth   I believe that
it is better judgment not to disturb the esophagus, but to do a
gastrostomy, this removes all irritation from the malignant
growth and gives an opportunity to properly nourish the patient
adding materially to the comfort

I have not discussed the treatment of diverticulum as it is
obviously surgical; nor pressure stenosis, for it is only amenable
to treatment when the underlying cause can be removed

CONCLUSIONS

First   That esophagoscopy can be done with very little dis-
comfort to the patient

Second   That esophagoscopy is a valuable aid in the dif-
ferential diagnosis in diseases of the esophagus

Third   That esophagoscopy is essential to the successful
treatment of cicatricial and spasmodic stenosis and ulceration
of the esophagus

Fourth   That esophagoscopy is the only safe means for
the removal of foreign bodies from the esophagus

CLINIC OF DR FREDERICK H BAETJER

Johns Hopkins Hospital

THE ROENTGENOLOGIC SIGNS OF JOINT LESIONS IN CHILDREN

Differential Diagnosis by the x-ray Between Rickets, Syphilis, Scurvy, and the Condition Known as Perthes' Disease

The object of this clinic is an attempt to systematize and if possible, arrange a classification of the various lesions of the joints of children from the changes that are seen upon an x ray plate.

All clinical signs were disregarded, and the study was based entirely upon data obtained from the x ray plate

The first factor obtained seemed to show that there was a fairly definite relation between the age of the patient and the type of lesion seen To one accustomed to studying x ray plates and one familiar with the development of the bony structure age can be determined from the x ray plate with a fair degree of accuracy

Accordingly, we found that the vast majority of lesions could be arranged roughly into three age periods

1 Those occurring from birth up to three or four years

2 Those occurring from three or four years up to seven years

3 Those occurring from seven years up to the adult age

In the first class we found that from birth up to one year tuberculous infections were so infrequent that they could be practically disregarded After one year, while tuberculous in fections occur, we do not begin to see them with any degree of frequency until we reach the third or fourth years In the same way, acute epiphysitis, while more frequent than tuberculosis, follows approximately the same course

In this period we will find that the joint changes are very largely confined to the lesions arising from rickets, syphilis, and scurvy

In the second age period we find that the three most common lesions of the first group have practically disappeared, to be replaced by the lesions of tuberculosis and acute non-tuberculous infections

In the third age period we have the lesions of period No 2 with one other added, namely, Perthés'

It must be remembered that the age classification is only approximate, and frequently the periods may overlap

Now let us consider the changes that take place with the lesions in age period No 1 Taking them up in the order of their frequency, we will first discuss rickets

We will first consider the changes that take place in the joints, and second, the remote or constitutional changes We find that there is multiple joint involvement There is fluid and swelling of the peri-articular tissues The cartilaginous surfaces of the joint are intact, but there is a marked disturbance of the epiphyseal line We find that the epiphysis becomes softened and has a tendency to spread out There is slight condensation at the epiphyseal line and the end of the bone has an inverted saucer-shape appearance (Figs 285, 286) The epiphysis proper is never disturbed and the changes are confined entirely to the epiphyseal line This saucer-shape expansion is most marked in the weight-bearing joints The most typical joints for diagnosis are the lower ends of the tibia and radius

Now since these joints are swollen and sometimes painful, there is limitation of motion, and, consequently, we get a general atrophy of the bones, not only due to disuse but also due to the fact that the disease is a nutritional one When the attack is especially severe and of long standing the atrophy becomes so extreme that the bones lose almost all their structure and are so seriously weakened that the slightest trauma will produce fractures In the severe cases multiple fractures are quite common

The writer has seen one case in which there were eighteen

fractures of the long bones, one bone, namely, the femur, having four distinct fractures   On account of the extreme atrophy we do not, as a rule, have periostitis, though occasionally it may be present to a slight degree
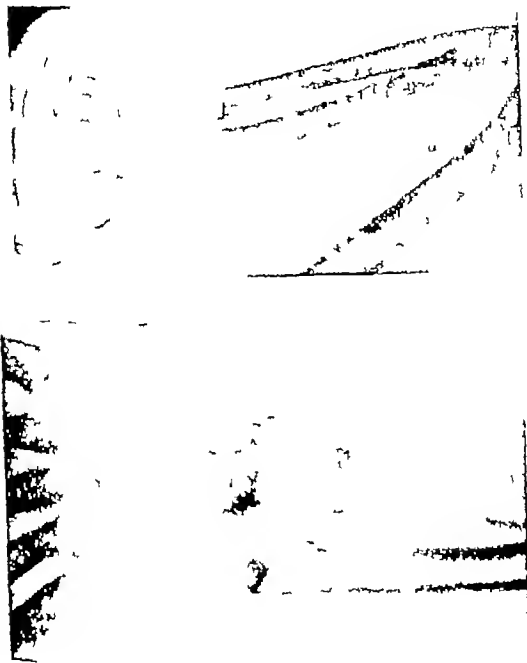
Figs. 285 286—Rickets Shows the periarticular swelling and the inverted saucer-shape appearance of the epiphyseal line, with bone condensation

Care must be taken not to mistake this condition for osteogenesis imperfecta   In this disease we have the marked atrophy and the multiple fractures, but the point of differential diagnosis rests upon the fact that there are no joint and epiphyseal changes

In the rachitic conditions it is always well to examine the chest, as we will find in typical cases the rosary at the ends of the ribs, due to the same saucer-shape expansion of the epiphyseal line of the ribs   Here again we get a secondary change in the lungs   We have spoken of the softening of the bones, due to the absorption of the calcium salts in the epiphyses   These two changes have weakened the costochondral region so very materially that, with the negative pressure in the chest coupled with the muscular pull of respiration, the costochondral region bends and is pulled in upon the lungs sometimes to such an extent as to affect the proper aeration of the lungs   We frequently find a band of consolidated lung just beneath the costochondral articulation which runs parallel to the sternum on each side   This consolidation is, in reality, an atelectatic strip from pressure, and is generally fatal

With proper treatment the epiphyseal changes clear up and there is frequently left behind a line of slightly condensed lime salts running across the bone, due to faulty calcification   The writer has on numerous occasions seen four or five such parallel lines, indicating that there had been that number of acute exacerbations in the course of the disease   When deformities have occurred such as those described in the bony structure of the chest or in bowing of the long bones, they, of course, invariably persist

It is well to mention that pulmonary complications are extremely common in rickets, due to the marked disturbance of the proper aeration of the lungs from costochondral pressure

To summarize the chief points
1   Occurs in the very young, especially first two years
2   Joint itself intact, spreading out of the epiphyseal line
3   Atrophy, with the frequent occurrence of fractures
4   Periostitis generally absent, though occasionally present
5   Marked pulmonary changes
6   No subperiosteal hemorrhages

In syphilitic lesions, just as in rickets, we have the joint and bone changes   The joints are generally multiple, there is sometimes periarticular swelling and fluid in the joint   The

always have more or less new periosteal bone   The chest and lungs are never involved   To summarize the chief points

   1 Occurs in the very young, especially in the first two years

   2 Joint itself intact, no spreading out of the epiphyseal line, but gouged out areas in the diaphysis

Fig 288 —Syphilis   Shows the gouged out area in the lower end of the humerus and slight periostitis

   3 No atrophy, and we seldom have fractures
   4 Periostitis almost always present and generally excessive
   5 No pulmonary changes
   6 No subperiosteal hemorrhages

Since rickets and syphilis are seen so frequently in the lower walks of life, these two conditions are frequently associated in

the same individual, and it is often difficult to determine from an s-ray standpoint which is the predominating factor in the case

In scorbutic lesions, just as in syphilis and rickets we have joint and bone changes The joints are generally multiple there is occasionally periarticular swelling and fluid in the joint
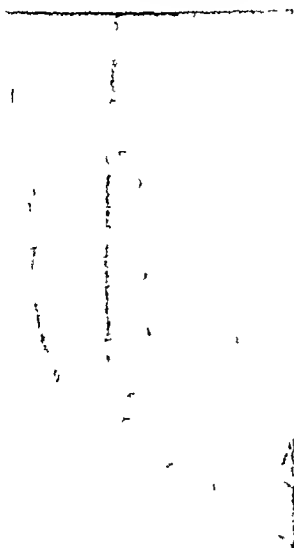
Fig 289—Scurvy Shows a huge organizing hematoma with definite calcium border, and the Trümmer' zone just behind the epiphyseal line of the femur and also beneath the epiphyseal lines of the tibia and fibula.

The cartilaginous surfaces of the joint are intact, but, like rickets and syphilis, there are marked disturbances in connection w⁻ the epiphyseal line All the changes take place upon the ⟨dia⟩-yseal side of the epiphyseal line The epiphysis and epip⁻ line are intact no changes taking place at all at these two There is no saucer-shape expansion of the end of the ⟨

rickets, or localized areas of softening and destruction as in syphilis. Just back of the epiphyseal line, from ½ to ¼ inch, is what apparently is a second epiphyseal line, which, in reality, is a band of localized destruction about $\frac{1}{10}$ inch in diameter, extending through the entire bone and parallel to the epiphysis. The edges of this band are frequently denser than the normal bone, and gives the appearance of eburnated bone, being due probably to the condensation of calcium salts (Fig 289). This band (Trummer zone) gives the appearance as if a surgeon had operated and taken out a cross-section of the bone.

Atrophy is sometimes present, but, on account of the periosteal bone fractures are infrequent. In this condition we have frequent hemorrhages beneath the periosteum which elevate the periosteum, and later there is organization of the hemorrhage (Fig 290). The organization produces such a hard tumor that the writer has seen 2 cases of this condition that were mistaken for sarcoma, especially after the acute scorbutic symptoms had subsided. The x-ray picture however, is so definite that once seen, a mistake in diagnosis will rarely be made.

To summarize the chief points

1 Occurs in the very young, generally in the first and second years

2 Joint itself intact. Epiphysis and epiphyseal line not disturbed, but the formation of this destructive zone behind the epiphysis

3 Atrophy occasionally present, but seldom fractures

4 Periostitis practically always present

5 No pulmonary changes

6 Subperiosteal hemorrhages frequently present

It will be noted in these three conditions—namely, rickets, syphilis, and scurvy—that they all occur at approximately the same age period and that the joint surfaces are intact. The differential points in diagnosis depend upon the changes in and around the epiphyseal line and the character of the periosteal changes

In rickets the changes are confined to the epiphyseal line, in syphilis the epiphyseal line and bone directly behind it are in-

volved, while in scurvy the epiphyseal line is intact and all the changes take place in the bone just behind it   In rickets there

Fig 200 —Scurvy   Shows a small hematoma and Trümmer zone at the lower end of the femur and the head of the tibia

is seldom periostitis, in syphilis there is marked periostitis while in scurvy the periostitis is frequently accompanied by sub periosteal hemorrhages

As we come to the close of this age period tuberculosis and acute epiphysitis of the joints become more frequent, and practically supplant rickets, syphilis, and scurvy in the second age period

In tuberculosis we find that the lesion is generally confined to one joint   There is periarticular swelling and fluid, but on account of the periarticular involvement the joint becomes very hazy and indistinct in the first stages of the disease   As the lesion progresses we begin to find that the articulating surfaces of the joint become irregular and worm-eaten and the bones forming the joint become very atrophic from disuse   The disease slowly destroys the cartilage and the bone beneath, but never metastasizes in the head of the bone, but proceeds by direct extension   As the disease subsides there is frequently subluxation, and when ankylosis takes place it is largely fibrous, there being but little bone production

In acute epiphysitis, non-tuberculous, it is frequently impossible to differentiate it from tuberculosis, except that, as a rule, the joint does not become as hazy and indistinct   The lesion is generally confined to one joint and the destruction is more rapid and the direct extension is more irregular   There appear frequently focal spots of disease in the bone not directly connected with the primary infection of the joint   As the disease subsides there is marked production of new bone, and the ankylosis is practically always bony in character

It will be noted that in the early acute stages of these two lesions it is frequently impossible to make a differential diagnosis, but when the stage of repair has been reached the marked production of new bone will indicate that the infection was pyogenic and not tuberculous

In this age period and the succeeding one we will occasionally see joints in which there is swelling and fluid   Repeated examinations at intervals will show that this type of joint is returning to normal   These must be looked upon as merely a synovitis produced probably by trauma, so slight as not to have been noticed

At the end of this second period and also part of the third

period we occasionally see that uncommon condition first described by Perthés In Perthés' original communication he described this lesion, and all of his cases were limited to the hip joint. In the writer's series of cases they were also confined to the hip-joint, and if they do occur in other joints, so far they have not been recognized
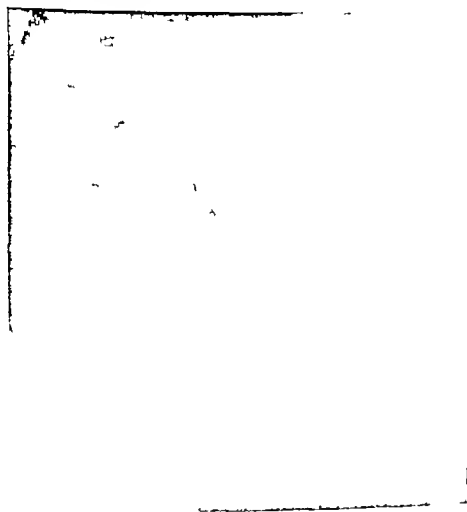
Fig. 291—Perthé s disease Shows the flattened eburnated epiphyseal head with a small fragment broken off

This condition is of peculiar interest in that all the signs and symptoms point to a tuberculous infection, but does not react to tuberculin, and recovery is much more rapid and the joint returns more nearly to normal The x ray picture when once seen is very typical   There is no hazing and clouding of the joint, the epiphysis is crushed down somewhat and flattened , and there is marked eburnation of the bone beneath the car

tilage, due to the packing down of the calcium salts, and occasion
ally small fragments may be broken off (Fig 291)   The le
sion may be unilteral or bilateral   The changes are entirely con
fined to the head of the femur, the acetabular surfaces appar
ently never being involved

With the union of the epiphyses we reach adult life, and then
comes that great arthritic group, namely, infectious, atrophic,
and hypertrophic arthritis   This group will not be discussed
since it is not in the province of this clinic

CLINIC OF DR LOUIS HAMMAN

Johns Hopkins Hospital

INTRODUCTORY REMARKS TO A DISCUSSION OF DIABETES

BEFORE commenting upon the cases of diabetes I have shown you I propose to review briefly the fundamental facts of carbohydrate metabolism. Every step in the treatment of diabetes and all of our clinical knowledge of the disease rests upon these facts. If you are familiar with them, then you know all there is to be known about diabetes, if you ignore them, you will never adequately appreciate the clinical problems this disease presents Let us then look upon the condition from this standpoint before we say a word about treatment.

called renal diabetes are consequent upon hyperglycemia, but the kidneys do not play an entirely passive rôle. Aside from instances of gross renal disease with impaired function, the permeability of the kidneys for glucose varies in different individuals and in the same individual at different times. However, the range of renal adaptability is relatively small. This constant blood-sugar level is maintained by a mechanism of great complexity which we are only beginning to understand. From the blood glucose is taken by the cells and utilized in the manufacture of complex substances forming an integral part of their structure, or stored as glycogen, or directly burned. As an integral constituent of cell substance glucose and its derivatives play an insignificant part in the animal economy as compared with their important rôle in plants. In the latter they are the chief constituents of the supporting and protecting tissues, whereas in the former these structures are protein in composition. Next to the liver, the muscles possess the main glycogen reserve of the body. Many other, indeed, perhaps all, cells possess slight glycogenic power. The burning of sugar is not a direct combustion. The decomposition to water and carbon dioxid is a slow progression through many complex chemical stages, the intricate nature of which has not yet been fully elucidated. If the supply of carbohydrate is abundant and all of the energy needs of the body are thereby covered and the glycogen reserve is complete, sugar may be further stored as fat. The weight of evidence points to the connective tissues as the seat where this conversion takes place. No matter what means we employ to reduce it, the glucose content of the blood is maintained desperately at its constant level. In starving animals it is reduced but little below the normal. If carbohydrate ingestion be greatly reduced or entirely suppressed, the animal organism will grasp its glycogen reserve, and, when this is exhausted, manufacture sugar from protein.

This brief statement of the essential and generally accepted facts of carbohydrate metabolism is offered merely as a loose framework upon which to hang more interesting details of the story

When carbohydrates are taken by mouth, if absorption proceeds slowly an unlimited amount can be utilized. In normal animals it is impossible to produce mellituria by feeding excessive amounts of starch. Even when disaccharids or monosaccharids are administered in conjunction with other food, sugar seldom appears in the urine. However, when sugar is taken into the fasting stomach, absorption proceeds with remarkable rapidity, and if large amounts are taken, sugar flows off in the urine. There is a wide individual variation in tolerance for sugar, but, on an average, 120 grams of glucose may be taken without producing mellituria. This "assimilation limit" for sugar is influenced by a great variety of conditions, and the interpretation of changes in the level is surrounded with difficulty, but its estimation is the first and a very important step in all clinical studies of carbohydrate metabolism.

This digestive factor in glycosuria is of practical importance. In all probability upon it depends the difference in the utilization of different starches. For instance, it is found in cases of severe diabetes that there is often distinct improvement in the assimilation of sugar when large amounts of certain carbohydrates are administered. Such improvement frequently follows an oatmeal cure. Evidence favors the view that the benefit of oatmeal depends largely upon the difficulty of digestion and the slowness of absorption.

If sugar absorption be sufficiently slow, nearly all of the sugar reaches the liver and there is built up into glycogen. When sugar in large amounts is given, but still below the assimilation level, glycogen formation often proceeds with such rapidity that the sugar content of the blood in the general circulation is temporarily reduced. It is possible that a small amount of sugar goes directly into the general circulation either through a failure of the liver to retain it all or, more probably, by way of the thoracic duct.

In well nourished individuals with a satisfactory glycogen reserve all of the ingested carbohydrate is not converted into glycogen, some is burned directly and some is converted into fat.

A more accurate way to test carbohydrate assimilation i.

by the alimentary route is to avoid the influence of digestion and absorption by injecting the sugar subcutaneously or directly into the blood-stream   Blumenthal found that rabbits became glycosuric following the intravenous injection of 1 gram of glucose per kilogram of weight, and that less sugar was needed for the purpose with dilute than with stronger solutions   After giving an amount just short of the assimilation limit, a second injection of even a very small amount promptly caused glycosuria   The prompt removal of a definite sudden increase in the blood-sugar Blumenthal calls the saturation limit, in contradistinction to the utilization limit which designates the utilization of a constant though moderate excess   The utilization limit he determines by injecting small amounts at frequent intervals. The saturation limit for glucose and levulose Blumenthal finds about equal, for galactose much lower, and for saccharose and lactose very low   Biedl and Kraus have injected from 200 to 300 c c of a 10 per cent. glucose solution in man without producing glycosuria or polyuria   Woodyat and his co-workers have amplified Blumenthal's observations in a striking way They have devised an instrument that will deliver a constant stream into the vein, and they find the utilization limit for glucose in a normal person to average 0 85 gram per kilogram per hour

Of the disacchands, maltose alone is utilized when injected directly into the blood   Saccharose and lactose are excreted almost quantitatively   It has been claimed that if these sugars are repeatedly injected, ferments gradually accumulate in the blood which split the disacchands, and the resulting monosacchands are then utilized   However, this claim has not been substantiated   As would be supposed from the galactose content of milk-sugar, saccharose is more readily utilized than lactose

By the subcutaneous method of testing the utilization limit for sugar, larger amounts are tolerated than intravenously   By this method it is found that galactose is less readily utilized than glucose or levulose, but in contradistinction to the results of the intravenous method glucose is much more readily utilized than levulose

As Allen has insisted, there is, strictly speaking, no true limit of tolerance for glucose   If the assimilation limit were real, then if a small amount of sugar were excreted after administering 150 grams of glucose, 50 grams should be eliminated after the ingestion of 200 grams of glucose   However, this is not the case, for no matter how much glucose above the tolerance limit is administered, but a small amount of the excess appears in the urine   Von Noorden gives the following data

Amount of glucose.	Healthy individual A excretes.	Healthy individual B excretes.
100 grams		
150 "	0 15 gram	
180 '	0.25	0 23 gram
200 "	0 26	0 71
250	0.52	0 64

Worm-Miller has these figures

After 50 grams of saccharose, 0 1 gram of sugar appeared in the urine.
After 100   "   0 85
After 250   "   1 8

Sugar introduced into the body parenterally is partly built up into glycogen, partly burned, and partly converted into fat. The body cells apart from the liver have a marvelous capacity for managing glucose   In frogs, extirpation of the liver does not reduce the tolerance for glucose   In geese, cutting off the portal circulation reduces but little the tolerance for glucose, but the levulose tolerance is considerably reduced   In dogs with Eck fistula the tolerance for glucose is unaltered, for levulose but little reduced, while galactose is excreted almost quantitatively   In rabbits, phosphorus-poisoning reduces the tolerance for levulose and for galactose, but not for glucose   Worner concludes from his studies that the tolerance for galactose runs parallel with the liver damage

In considering the relation of the liver to glycogen, it is useful to distinguish three functions   (1) The formation of glycogen from sugar—glycogenesis, (2) the breaking down of glycogen into glucose—glycogenolysis, (3) the formation of glycogen

cogen from substances other than carbohydrates—glyconeo genesis

Glycogenesis   Under normal conditions the liver manufactures glycogen from the sugars that reach it through the portal circulation   Under carbohydrate feeding its store of glycogen may reach fully 15 per cent of the total weight   The exact mechanism of glycogen formation is not understood   There is a very definite enzyme in the liver and in other tissues of the body and in body fluids that splits glycogen into glucose   Since the reversible action of enzymes is a common biologic phenomenon, it has been assumed that glycogenase may build up as well as break down glycogen   Cremer thought he obtained evidence of glycogen formation by mixing yeast juice and glucose, but his results have not been confirmed   Indeed, innumerable attempts to produce glycogenesis with glycogenase and other ferments have failed   It has been suggested that sugar undergoes some chemical change either by enzyme or hormone action before being condensed to glycogen, but the evidence is inconclusive   Nor is there conclusive evidence from which to decide whether this function is stimulated directly or is under the influence of nervous control   The technical difficulties of perfusion experiments render the results questionable   The fact that adrenalin while producing hyperglycemia and glycosuria, still, at the same time, causes an accumulation of glycogen, suggests that at least some nervous control is exercised

It has been thought that glycogen is not produced from the different sugars in exactly the same way   In dogs with pancreatic diabetes, Minkowski found that there was a storing of glycogen and an improved carbohydrate metabolism after levulose, while no glycogen formation followed glucose administration   Von Noorden is convinced that similar conditions obtain in man, and upon this authority the difference has been made much of in the treatment of diabetes   Some years ago Magnus-Levy expressed the conviction that in severe cases of diabetes there was no apparent difference in the behavior of the two sugars, and recently Minkowski's experimental work has not been confirmed

Glycogenolysis, as has been stated, is directly produced by the enzyme glycogenase This enzyme is found in the liver and in all the body tissues and juices Whether it is formed in the tissues or appropriated by them from the body juices is undetermined It would appear that mainly the pancreas furnishes the blood and lymph with glycogenase All attempts to identify variations in glycogenase as responsible for abnormalities in carbohydrate metabolism have failed MacLeod has shown that glycogenolysis caused by stimulation of the splanchnic nerves proceeds without change in the amount of glycogenase. Further studies led him to conclude that the process depends upon the reaction in which the enzyme works, its activity being greatly increased in a slightly acid environment Glycogenolysis proceeds with great rapidity when the liver is removed from the body and after death However under normal conditions it is largely under nervous control, and this mechanism involving the reciprocal and antagonistic activities of the various endocrine glands is one of the most fascinating chapters in recent medical discoveries

Glyconeogenesis is intimately bound up with glycogenolysis Whenever the body demands a fresh supply of sugar the glycogen reserve of the liver is called upon The muscles and probably other tissues hold their glycogen more tenaciously As the glycogen reserve in the liver is diminished, a fresh supply is built up from the carbohydrates of the food, and if these are not available, sugar is formed from protein and perhaps from fat. Under all conditions, even in extreme starvation, the body fights to keep its blood sugar at a constant level This effort is apparently as fundamental and far reaching as the attempts to maintain a constant reaction and salt equilibrium Pflüger was the powerful opponent who held out so long against admitting the formation of sugar from protein, but shortly before his death he realized the absolute necessity of its recognition and added valuable evidence to its support. Study upon patients with diabetes and upon diabetic animals has shown that the amount of sugar produced cannot be accounted for by the glycogen reserve of the body and the carbohydrate ingested

During starvation and when fed solely upon protein completely diabetic animals manufacture sugar from protein in a constant proportion If all of the carbon in protein were converted into sugar, then for each gram of nitrogen 8 grams of sugar would be formed It is remarkable that in pancreatic diabetes in dogs during starvation or upon a wholly protein diet the nitrogen-dextrose relation is constantly in the neighborhood of 2 8, in phloridzin diabetes under similar conditions it is 3 6, when pancreas and thyroid are both removed, it is said also to equal 3 6 Lusk has accepted 3 6 as the maximum sugar formation from protein It has been objected to these figures that in estimating the urine nitrogen no account is taken of the endogenous or cellular nitrogen metabolism It is assumed that all protein is converted into sugar Corrected in accordance with these views, the dextrose-nitrogen ratio in pancreectomized dogs is 3 3, in phloridzin and severe human diabetes, 6 Gigon regards 6 as the maximum figure and refuses to recognize higher values that have been reported in man by Falta and others

Not all portions of the protein molecule furnish sugar with equal facility Although it would seen reasonable to select glucosamin as the readiest source of sugar, all investigations with this derivative indicate that it is not utilizable in this manner The work of Embden and of Lusk has shown that certain of the amino-acids, for instance, glycocoll, alanin, as-'uc acid, and glutamic acid, readily form sugar, while others, instance, leucin and tyrosin, do not Apparently, those amino-acids that fail to yield sugar are easily changed into the acetone bodies All of the carbon atoms of glycocoll and alanin are directly convertible into sugar, while but three of the four carbon atoms of aspartic acid and three of the five of glutamic acid are susceptible of such transformation The experiments of Embden make it altogether probable that at least the main stage in the conversion of the amino-acids into glucose takes place in the liver

It is a matter of great practical importance to know if all proteins are equally sugar yielding Such information might

point valuable lessons in the treatment of diabetes It has been found that of all proteins, casein yields sugar most readily This has been explained by the ease and rapidity with which casein is split in the intestinal canal, the body being thus flooded with amino-acids This is a reasonable explanation and is supported by analogy with carbohydrate utilization, slow digestion and absorption facilitating its conversion into glycogen Rolly and Oppermann find in diabetes that meat and aleuronat, a vegetable protein, affect the glycemia and glycosuria equally, except that when the latter substance is administered, the rise in sugar occurs later and endures longer They ascribe the difference to the delayed digestion and absorption of the vegetable protein.

Estimating the amount of sugar that might come from carbohydrates and proteins, certain authors find in severe diabetes an excess which they conclude must come from fat. Feeding experiments have proved conclusively that glycerin is convertible into sugar, but even allowing for this constituent of fat there is still a deficit which they believe is derived from the fatty acids. The question is still unsettled and has given rise to a lively controversy

It is needless to comment upon the important place the liver occupies in carbohydrate metabolism However, the present attitude is to regard it as a passive organ yielding its supply of sugar and manufacturing fresh material under the pressure of outside influences With the exception of phloridzin and pancreatic diabetes all other clinical and experimental forms of glycosuria depend in large measures upon the glycogen content of the liver Even in phloridzin and pancreatic diabetes since the liver is the only, or at all events the principal, site of glyconeogenesis, glycosuria depends upon its integrity Pflüger justly says without the liver there can be no diabetes. In frogs if the liver be removed, extirpation of the pancreas causes no glycosuria. Hedon finds that pancreas extract injected into the portal circulation of dogs with pancreatic diabetes striking effect upon the glycosuria, whereas, injected i general circulation, it has no influence If these r

confirmed, they would indicate that the liver in some way activates the pancreatic secretion

Glycogenesis is such a fundamental function of the liver that its exercise is continued under the most adverse conditions   In starving animals, the liver builds glycogen up to the time of death, and even in severe diabetes the property is not totally lost   It is probable, then, that this function would be seriously impaired only in extreme hepatic disease   Clinical evidence supports this view   Cirrhotic and parenchymatous lesions are frequently found in the livers of diabetics, but all investigators agree in regarding them as secondary to and not the cause of the disease   The striking increase in Kupffer cells reported by Fisher and the nuclear distribution of glycogen noted by Huebschmann are interesting pathologic findings, but have no casual relation to the disease   There has been a lively controversy between clinicians as to the existence of purely hepatic diabetes   French authors continue to describe such cases, but the condition has neither firm clinical nor experimental evidence for its support, and the majority of clinicians refuse to recognize it

Since the discovery of the glycogenic function of the liver by Claude Bernard, sugar tolerance has been used as a test of hepatic function   The French school has claimed great clinical value for the test, while German authors have with equal firmness rejected it as useless   Straus in 1898 thought he had discovered the reason for this discrepancy   The French clinicians had been using 150 grams of cane-sugar, the Germans, 100 grams of glucose, in performing the test   Straus found that these sugars are not utilized with equal facility, and attributed the difference to the levulose in cane-sugar   He, therefore, devised a test of liver function, using levulose as a test-meal   The sum of clinical investigation shows some relation between liver injury and levulose assimilation, but authors disagree widely in their opinion of the clinical value of the test   Churchman, after a study of cases in the wards at the Johns Hopkins Hospital, concludes the test has little clinical value   Since experimental results indicate that galactose is handled exclusively

by the liver, Bauer proposed substituting galactose for levulose in testing liver function, and claims this change gives far better results. Bloomfield and Hurwitz give a good account of the difficulties surrounding the interpretation of these tests

In the past few years interest in abnormal carbohydrate metabolism has been transferred largely from glycosuria to a study of the behavior of the sugar in the blood   Simplified methods of determining blood-sugar have facilitated clinical studies.   In normal animals and in man it is found that the sugar content of the blood varies somewhat in different parts of the circulation   Lepine finds a higher content in the carotid artery than in the right auricle   Slight muscular exercise may increase, severe exertion reduces it   There is a well marked rise after bleeding   Fever increases it.   Various pathologic conditions, as nephritis, disease of the liver and intestines, anemia, and so on, influence it.   It is increased by dyspnea, asphyxia, narcosis, and emotional conditions   Of special interest, however, is the relation of blood-sugar to carbohydrate digestion   It has long been known that alimentary glycosuria is often the earliest manifestation of beginning diabetes, and the behavior of the blood-sugar following carbohydrate ingestion, therefore, acquires special significance   In animals and in man the ingestion of sugar following a short period of starvation is followed after fifteen minutes by a definite rise in the blood sugar, after one hour the amount is almost doubled, the hyperglycemia then gradually subsides and disappears at the end of three hours.   In well fed animals the rise is slower and less marked, and if tests be made in quick succession, each repetition is followed by a less decided change, until the effect is lost completely   Starch and certain vegetables have the same effect as glucose when administered upon an empty stomach, but the effect is diminished in proportion to the admixture of other foods.   In man, bread eaten with butter has a much less decided influence upon the blood-sugar than bread alone   The digestive factor in carbohydrate metabolism has been pointed out.   These studies in digestion hyperglycemia give us valuable

clinical hints for dietetic management of diabetes   Protein digestion has no influence upon the blood-sugar

The condition in which sugar exists in the blood has given rise to much speculation   Reduction tests give larger amounts than polarization   The difference may be explained by the small amounts of levulose, maltose, pentose, and glycuronic acid that are sometimes present   All of these reducing bodies normally found in blood are grouped by Lepine as "sucré immediat" If blood be mixed with acid and heated and the sugar then estimated by reduction, a larger amount is found than before This bound sugar Lepine calls "sugar virtuel"   There is at present no value attached to these differences, and when blood sugar is spoken of the "sucre immediat" is meant

Since the blood-sugar dialyses in a normal way, it has been assumed that it exists free in the blood   On the other hand, many authors insist upon speculative grounds that the assumption of some form of loose combination is necessary to fit facts satisfactorily into any reasonable plan of sugar metabolism   Allen is the latest and most forceful of these advocates   He assumes that sugar before entering into the blood-stream combines with another substance, the resulting body having colloidal properties   This combining substance he calls, in terms of the well-known immunologic nomenclature, amboceptor   He assumes that the pancreas is directly responsible for the presence of this amboceptor, the absence of which is the cause of pancreatic diabetes

Regulation of the sugar content of the blood is a fundamental property of the body   The regulating mechanism that guards against an excess of sugar resides partly in the tissues themselves   The early fall of postprandial hyperglycemia may be due in part to absorption of water from the tissues, for the hemoglobin often falls as the sugar proportion decreases At the same time the tissues become saturated with sugar However, a more important part of the regulatory mechanism resides in the kidney   When hyperglycemia reaches a certain level, sugar flows off in the urine   In this sense the kidneys may be likened to the overflow pipe of a cistern, but the compari-

son is only superficial, for their action is by no means passive Under normal conditions glycosuria and hyperglycemia run fairly parallel However, in diabetes there is by no means such a constant relation, for the relation varies in different individuals and in the same individual at different times There is often marked glycosuria when the hyperglycemia is below the level frequently exceeded in normal individuals without loss of sugar in the urine. Indeed, in some severe cases of diabetes the blood-sugar is surprisingly low In diabetic coma there is frequently an abrupt diminution in the urine sugar, while the blood-sugar ascends to a very high level As is well known renal disease seriously affects the organ's permeability for glucose In diabetes, when nephritis develops, glycosuria may entirely disappear, while the blood sugar proportion increases Experimental nephritis following injection of the salts of uranium and chromium frequently is associated with increased permeability and glycosuria Luthje reports a patient developing glycosuria with the onset of a renal lesion MacLeod has shown that the rate of blood flow in the kidney has a decided influence on sugar excretion. Such considerations make apparent the clinical value of blood-sugar determinations. These may prove to be not only our safest guide to the early diagnosis of diabetes mellitus, but likewise our most reliable source of prognostic and therapeutic information throughout the course of the disease

Although the kidneys do not play an entirely passive rôle in glycosuria, still, with few exceptions, glycosuria is always secondary to hyperglycemia The exceptions are the galactosuria of pregnant women, certain cases of so-called renal diabetes, and phloridzin diabetes. Experimentally phloridzin diabetes is the only true renal glycosuria. In starvation and upon a protein diet sugar is excreted in a constant proportion, the nitrogen-dextrose ratio being 3 6 Not only is there no hyperglycemia, but the blood sugar is greatly reduced The glycosuria in no way depends upon the glycogen content of the liver, for it occurs with equal intensity during inanition It increases the glycosuria in animals with pancreatic diabetes, and such animals almost at the point of death and free from

glycosuria on account of advanced weakness again eliminate sugar from phloridzin influence. In severe phosphorus-poisonings it still causes glycosuria. Temperature and muscular exertion have no influence upon its action.

In man rare cases of glycosuria are distinguished by an absence of any relation between carbohydrate ingestion and sugar elimination, by an absence of hyperglycemia, and by their failure to develop under prolonged observation any of the usual symptoms of diabetes mellitus. Such cases have all the characters of a true renal glycosuria, although some experienced observers refuse to recognize renal diabetes as a clinical entity. There is good evidence for considering the galactosuria of nursing women a pure renal mellituria.

Of all the regulators of carbohydrate metabolism, the pancreas has held and still holds the point of highest importance. Removal of the organ in animals causes a severe glycosuria which persists whether sugar be given or withheld. In starvation or on a protein diet sugar is excreted in a constant proportion, the dextrose-nitrogen ratio being 2.8. The animal rapidly emaciates, acetone bodies appear in the blood, and death occurs in from two to four weeks. Besides the failure to utilize sugar there is also a profound change in the general metabolism. The hunger protein metabolism is increased threefold and fat consumption is likewise increased. This remarkable influence that the pancreas exercises upon carbohydrate metabolism is due to some substance secreted in the blood-stream, for the pancreatic duct may be tied off or transplanted so that the secretions are poured upon the surface of the body and no change in sugar metabolism occurs. When a small piece of the pancreas with the blood-supply intact is transplanted subcutaneously, glycosuria does not occur; when the graft is subsequently excised, diabetes promptly sets in.

Of still greater clinical interest than total extirpation of the pancreas are the results of partial removal. These experiments were first performed by Sandmeyer, and the condition has since been known as Sandmeyer's diabetes. When small portions of the pancreas are allowed to remain and the ducts are

tied, the animals at first do not become diabetic, but as the remaining portion of gland degenerates, glycosuria develops, and finally the picture following complete removal of the organ supervenes. Allen has shown that when a small portion of the pancreas is allowed to remain in communication with a patent duct, a balance is often struck, so that the animals are glycosuric after carbohydrate ingestion, but the urine remains sugar free on a protein and fat diet. In dogs and cats he has made the remarkable observation that the ultimate outcome of this mild diabetes may be completely controlled through the diet. If, on the one hand, animals are liberally fed with carbohydrate, the diabetic condition progressively increases, so that later they excrete sugar when given only protein food, and finally they emaciate and die a typical picture of fatal diabetes. If, on the other hand, the animals are fed upon a protein and fat diet, they are maintained in good condition, and not only is fatal diabetes avoided, but, indeed, after a certain period it is found that their tolerance for carbohydrate has increased. The practical importance of these observations needs no emphasis. It is the first solid experimental evidence to support the methods of treatment that clinical observation has already established.

It has long been assumed that the action of the pancreas upon carbohydrate metabolism is due to an internal secretion. There is much presumptive evidence in favor of this view. Transplantation and partial extirpation experiments can scarcely be explained upon any other assumption. However, it must be admitted that so far satisfactory evidence of the presence of an internal secretion has not been submitted. On three occasions we have thought that such evidence had been obtained, but in each instance disappointment quickly followed. Lepine in 1890 discovered that the disappearance of sugar from drawn blood was due to a glycolytic ferment which was bound to the leukocytes. Further experiments led him to believe that the ferment was greatly diminished in diabetes. Subsequent observations have disproved Lepine's impressions, and it has been pointed out that the glycolytic ferment in blood is too small in amount to adequately explain the normal combustion of sugar

Cohnheim in 1903 found that whereas fresh extract of pancreas or muscle juice has little effect in destroying sugar, the two combined have marked glycolytic power   The simplicity and far-reaching importance of this discovery gave it wide acclaim   The studies of Claus and Embden and of Simpson have proved the results to be fallacious   Knowlton and Starling in 1912 found that the heart from a normal animal perfused outside of the body consumed more sugar than did the heart from a diabetic animal, and that the power of the isolated diabetic heart to consume sugar was improved by the addition of pancreatic extract to the perfusion fluid   In a series of convincing experiments MacLeod and Pearce failed to confirm these results   Starling has subsequently pointed out the source of error in his first experiments However, the same question has been raised again by the work of Admont Clark   Clarke has shown that the utilization of sugar by the perfused living heart is greatly increased if the perfusion solution is first passed through the pancreas   The pancreas seems to supply something to Locke's solution circulating through its arteries which in some way brings about a better utilization of sugar   This pancreatic substance possesses some of the properties of an enzyme

A conclusive proof of an internal secretion from the pancreas has been sought in the influence of normal blood which presumably contains this secretion and of pancreas extracts upon diabetes   The results of experiments undertaken with blood from the general and from the portal circulation have been negative   Some observers claim to have obtained evidence of improvement in sugar utilization, but their claims have not been confirmed

The recent work of Verzar and of Murlin and Kramer firmly establish that pancreatic extracts are no more effective   The conditions in the parabiosis experiments of Sauerbruch and of Forschbach are too complicated to permit of undisputed deductions   By uniting the circulations of a normal and a diabetic dog the authors observed a decrease of glycosuria in the diabetic animal, although the normal animal became glycosuric Hedon made the interesting observation that when the pancreas

of a normal dog with its vascular attachment preserved is transplanted between the carotid artery and jugular vein of a diabetic dog the glycosuria remains uninfluenced. However, when the anastomosis is made with the splenic artery and vein, the glycosuria is greatly decreased, to return with the former severity when the animals are separated. Hedon then found that though blood from the pancreatic vein of a normal animal injected into the general circulation of a diabetic animal did not appreciably influence the glycosuria, when injected into a mesenteric vein the glycosuria was markedly decreased. The technical difficulties of such experiments are so great and the conditions surrounding them so complex that inferences must be drawn with great care. The implications of Hedon's experiments are obvious, but so far as I know the observations have not been confirmed.

It is generally conceded that the source of the pancreatic influence over sugar metabolism resides in the islands of Langerhans. Schaefer suggests this view in 1895, and it was elaborated by Opie. However, there is by no means accord upon this point among pathologic anatomists. Hansemann still champions the acinous theory, although he stands alone, while those authors with widest experience—Opie, Weichelsbaum, Sauerbruch, MacCallum and many others—adhere to the insular theory. In recent years prominent pathologists, among them Reitmann, Herxheimer, Fahr, have accepted the view that the islands of Langerhans do not represent independent structures. They find so many transition forms between acini and islands that they believe one may under certain conditions be transformed into the other. Perhaps the strongest support of the island theory was the observation that tying the pancreatic duct which does not produce glycosuria leads to atrophy of the acini, but leaves the islands intact. However, Pratt finds the islands degenerate as well as the acini, and though glycosuria does not develop, sugar tolerance is reduced. Homans has recently added valuable evidence to the island theory by studying the islands in the piece of gland left after partial removal of the pancreas in cats. In those animals which fail to devel-

diabetes the disappearance of secretory granules in the islands suggests overactivity, in those developing diabetes he finds degeneration of the islands without disturbance of the remaining acinous tissue Embryologic and histologic studies indicate the structural independence of islands and acini

In pancreatic diabetes there is both an increased production of sugar and a loss of the tissue power to utilize sugar, but which of the two is the primary and essential factor has long been controverted That sugar introduced subcutaneously is quantitatively excreted and the constant dextrose-nitrogen ratio point against any utilization of sugar However, certain arguments have been advanced in favor of a partial combustion in pancreatic diabetes First, sugar given by the mouth is not always quantitatively excreted It is possible that some sugar is lost by decomposition or remains temporarily stored in the body At any rate, the force of this argument is lost, since calorimetric experiments fail to indicate any rise in the respiratory quotient Second, phloridzin and adrenalin increase the glycosuria This argument is hardly of importance, since the mechanism of phloridzin and adrenalin diabetes is not fully understood It is quite probable that their point of attack is different from that of the pancreas Third, the failure of acidosis in depancreatized dogs Brugsch particularly has pointed to this as the chief distinguishing feature between human and experimental diabetes In this statement the different dietary habits of man and dog are not sufficiently weighed, and later experiments have shown that acidosis is by no means rare in dogs Fourth, muscular exercise decreases the glycosuria and raises the respiratory quotient Seo has shown that this occurs only when the pancreas has not been totally removed Fifth, cold increases the glycosuria Allard fails to confirm this observation, and Luthje explains it by assuming an increased production of sugar from protein which is then excreted instead of being burned

All of the evidence then points against any sugar utilization in the tissues of animals with pancreatic diabetes, and these results have been established likewise for severe diabetes in man Whether this inability to utilize sugar resides in the tis-

sues themselves or in some alteration in the sugar that is presented to them remains undetermined. Porges and Solomon found that after cutting off the circulation below the diaphragm of pancreëctomized dogs, the respiratory quotient rose to one—indicating that sugar was then being burned in the muscles. They explain the constantly low respiratory quotient in diabetes by assuming that during the transformation of protein and fat into sugar, bodies with a very low respiratory quotient are formed, and though sugar is burned in the tissues, still these bodies hold the quotient down. Since the liver is the organ where protein and fat conversion into sugar occurs, eliminating the liver immediately raises the quotient to the sugar level. The main importance of this experiment is that von Noorden gives it prominence in his latest theory of diabetes. However, the results of Porges and Solomon lose all value before the withering criticism of Rolly and David.

Pancreatic diabetes is the only experimental form of glycosuria that bears any similarity to the disease diabetes mellitus. However, a consideration of pancreatic influence by no means exhausts the possibilities of carbohydrate metabolism, for although the pancreas is the dominant regulator, other glands play a not insignificant rôle.

Blum in 1901 noted glycosuria after the subcutaneous and intravenous injection of epinephrin. Subsequent observations have shown that the glycosuria lasts as long as epinephrin is present in the blood, and that the degree of glycosuria is roughly parallel with the epinephrin concentration. Subcutaneous and intraperitoneal injections cause a more marked glycosuria than intravenous injections, but a continuous inflow of very dilute epinephrin will establish and maintain glycosuria. After continuous or repeated injections glycosuria fails to occur, although hyperglycemia persists. Pollock ascribes this to changes in renal function. Epinephrin produces its most marked effect when a glycogen reserve is present, but it causes glycosuria in starving animals and increases the glycosuria at the height of pancreatic diabetes and in human diabetes. However, if the pancreas and adrenals are removed in dogs glycosuria does not

occur It is said that under the influence of epinephrin the muscle glycogen disappears before the liver glycogen, which is the reverse of all other forms of glycosuria Epinephrin causes glycosuria in fasting dogs This sugar is formed from protein, and Eppinger, Falta, and Rudinger have demonstrated an increased protein katabolism However, Ringer and Lusk have been unable to confirm this observation In contradistinction to pancreatic diabetes, the hyperglycemia caused by epinephrin is associated with an increased combustion of sugar Paton states that while glucose facilitates the action of epinephrin, levulose has not the same effect In dogs with the adrenals removed and in Addison's disease there is a low blood-sugar, increased tolerance for glucose, and an absence of glycosuria after epinephrin

The point of action of epinephrin is certainly upon the terminals of the sympathetics in the liver This is in accord with the general law of its action It is further supported by the observation of Loewis, that chrysotoxin which inhibits the sympathetic control likewise inhibits the action of epinephrin and that ergotoxin also diminishes its action MacLeod and Pearce have shown that a stimulation of the splanchnics causes hyperglycemia, if the adrenals are removed or the liver completely denervated, hyperglycemia does not follow such stimulation Therefore, they conclude that while epinephrin is absolutely necessary for stimulation of the splanchnics to be effective, still the effects of stimulation depend upon something more than an increased discharge of epinephrin

Similar to the effect of the adrenals upon carbohydrate, tabolism is the action of the hypophysis Injections of the act cause glycosuria, increased protein katabolism, and a in the respiratory quotient indicating sugar consumption shing and his co-workers have shown that electric or mechanical stimulation of the hypophysis causes glycosuria, followed by a period of decreased carbohydrate tolerance, and that removal of the gland is followed by increased sugar tolerance and a tendency to put on fat

Eppinger, Falta, and Rudinger have given a prominent place

to the thyroid and parathyroid glands in carbohydrate metabolism In thyroidectomized dogs they find the protein metabolism reduced and the protein-saving qualities of sugar and fat diminished, feeding thyroid again increases the protein metabolism and restores the normal protein-sparing property of sugar and fat The glycosuric action of epinephrin is lost, but is again restored by prolonged thyroid feeding Phloridzin acts quantitatively and qualitatively as in normal dogs In contradistinction to the effects of removal of the pancreas alone, removal of the thyroid and pancreas leads to no increase of protein metabolism, the dextrose nitrogen ratio equals 3.5, and the loss of weight of hungering animals is less rapid In thyroidectomized dogs, piqure fails to produce glycosuria The parathyroids, according to these authors, have an action opposed to thyroid If parathyroids and thyroid are removed, epinephrin produces glycosuria as normally and the assimilation limit for sugar is greatly decreased If the parathyroids alone are removed, there is a great reduction in sugar tolerance and the protein metabolism remains unaffected When the pancreas and several parathyroids are removed, the dextrose-nitrogen ratio rises to 3.5—but in contradistinction to the conditions following pancreas and thyroid removal, the protein metabolism is increased as it is when the pancreas alone is removed In the pancreas-thyroid experiments the amount of sugar excreted was the same as when the pancreas alone was removed, and Eppinger, Falta, and Rudinger explain the high dextrose nitrogen ratio by the lowered protein metabolism due to the removal of the thyroid These results upon the influence of the thyroid and parathyroid upon carbohydrate metabolism have been severely criticized Underhill and Saiki found that dogs with the thyroid removed tolerated little sugar subcutaneously, results which Eppinger, Falta, and Rudinger insist are due to removal of the parathyroids with the thyroid Underhill has produced epinephrin glycosuria in thyroidectomized dogs with two parathyroids remaining Ritzmann claims that the loss epinephrin glycosuria is only one of the many immediate effects thyroidectomy, and that after a few days the glycosuric pro

of epinephrin is restored On the other hand, McCurdy finds that if the thyroid be removed and the parathyroids remain there is a permanently increased tolerance for sugar, and Mac-Callum's experiments indicate a reduction in the glycosuria of pancreëctomized dogs when the thyroid is subsequently removed

In all experimental work in diabetes and perhaps still more strikingly in clinical observations the importance of a nervous element in glycosuria has been recognized Claude Bernard showed that a stab into the floor of the fourth ventricle at the apex of the calamus scriptorium caused transient glycosuria The results of the piqûre depend upon the glycogen reserve in the liver, for if the liver be rendered glycogen-free, glycosuria fails to appear The impulse from the brain to the liver is conducted through the sympathetic, for section of the sympathetic cord prevents glycosuria after piqûre Further, it has been found that section of the left splanchnic prevents glycosuria just as section of the sympathetic cord does The left splanchnic supplies both adrenals When the adrenals are removed, piqûre is without effect This evidence implicating the adrenals as an essential link in the mechanism of piqûre glycosuria is further supported by the observations of Stewart, who finds an increased outflow of epinephrin from the gland after splanchnic stimulation, and the histologic studies of Kohn, which point to increased activity of the chromaffin cells after splanchnic stimulation Evidence from older experiments indicates that piqûre is effective when all the nerves to the liver are cut, but MacLeod and Pearce have shown that when the denervation is complete splanchnic stimulation only occasionally leads to erglycemia Therefore, while epinephrin is apparently essential for sugar mobilization, still these authors think splanchnic stimulation exercises a direct influence upon the liver

Of the greatest importance are the studies of Cannon and his co-workers, who find emotional states such as fright are accompanied by an increased secretion of epinephrin, and not infrequently with glycosuria

The whole question of nervous glycosuria and particularly of the glycosuria associated with cerebral injury and disease needs

revision in the light of Cushing's experiments upon the hypophysis. As he has pointed out, the Claude Bernard piqûre is very close to the hypophysis, and puncture of the hypophysis has the same effect as the classical piqûre. Stimulation of the superior cervical sympathetic ganglion causes glycosuria even if all possible paths of downward conduction are cut, and even after connection with the central nervous system is destroyed by nicotin. When the hypophysis is removed, stimulation of the superior cervical sympathetic ganglion fails to give glycosuria. A Bernard piqûre will cause glycosuria even after transection of the cord above the emergence of the splanchnics. The general experimental evidence would indicate that under nerve stimulation the adrenals react more promptly than the hypophysis in producing glycosuria, but that the latter gland may function in the same way as the chromaffin tissue does. What interrelation there may be in their function remains unexplained.

On the basis of the interaction of the ductless glands in regulating carbohydrate metabolism an elaborate theory of diabetes has been erected. Much of this work has been done by von Noorden's pupils and it has received the stamp of his approval. The theory is applied in detail in the last edition of his book on diabetes. A fundamental basis of the conception rests upon the experiments of Porges and Solomon which have been recorded. The deduction from the experiments is that the diabetic organism is able to burn sugar just as the normal organism does, and that experimental pancreatic diabetes, as well as the disease in man, is primarily an overproduction of sugar and not an inability to utilize it.

Normally, the glycogen reserve of the liver is consumed in response to the needs of the body, and as the glycogen is used up, a fresh supply is manufactured from the food. The pancreas is the great controller of this process, the damper that holds it within appropriate bounds. When its regulating influence is removed, sugar production goes on in an unrestrained and inordinate way, the blood is flooded with glucose, and sugar flows off in the urine. The chromaffin system is the important sugar

mobilizer Its action is opposed to that of the pancreas Normal carbohydrate metabolism is the result of a balance between these two forces Nervous influences play an important part by stimulating the adrenals and other endocrine glands play their part by either exciting or depressing the function of the pancreas or adrenals Thus, the thyroid augments the adrenals, while it inhibits the pancreatic function Therefore, when the thyroids are removed, pancreatic glycosuria is diminished, when the gland is hyperactive, glycosuria readily occurs Reversely, if the pancreas be removed its depressing action upon the thyroid is released, the thyroid then forcing up the general metabolism and thus producing the increased protein metabolism characteristic of pancreatic diabetes In like manner the relation of the parathyroids and of the hypophysis in this schema may be easily deduced In a broad way the pancreas and parathyroids presumably depress carbohydrate metabolism, while the chromaffin tissue, thyroid, and hypophysis facilitate mobilization Diabetes, therefore, is no single entity, for if any chain in this complex system of regulation be impaired, the co-ordination of activity of all the endocrine glands is deranged

There is no evading the fascination of this hypothesis, and though persuaded of the inaccuracy of much of its foundation, still it is difficult to disregard its charm It lends itself admirably to diagrammatic representation, it allows of complex and yet clear explanation of many of the otherwise unexplained facts of carbohydrate metabolism, and it encourages endless even though vague and fanciful speculation It is well to insist, as has been already pointed out, upon the firmly established fact at the primary and essential feature of diabetes is an inability utilize sugar All else is secondary to this deficiency The hyperglycemia, the glycosuria, the glycogen depletion, and increased glyconeogenesis are in response to a constant demand of the tissues for more sugar which they cannot use What part the endocrine glands other than the pancreas may play in this fruitless and distorted mobilization is still undetermined

Although the explanation of the nature of diabetes upon the basis of interaction of the endocrine glands is quite inadequate

to meet the facts, still the observations that have been made upon their influence upon metabolism have shed considerable light upon their function and have given valuable points to the clinical interpretation of their derangements. Individuals normally vary in their response to alimentary tests of sugar tolerance, but the range of variation is relatively small, and any gross departure from the usual limits has an important clinical significance. A tolerance reduced so low that sugar occasionally appears in the urine upon an ordinary diet does not always mean diabetes. It is true that the distinction here requires the most refined clinical interpretation, for diabetes no doubt often begins as an alimentary glycosuria, and passes gradually through the stage of glycosuria following starch ingestion, and finally to glycosuria upon a purely protein diet. The importance of early diagnosis in diabetes I have sufficiently emphasized, but the stress will bear repetition, since there is every reason to believe that judicious dietary management will postpone and in some instances possibly avert the later and serious stages of the disease. But occasional glycosuria should prompt us to review carefully all possible sources of carbohydrate metabolism derangement, and a suspicion of disease of some of the endocrine glands may find considerable support from an estimation of the glucose tolerance. As a rule, decrease of carbohydrate tolerance is accompanied by loss of weight, and an increase by an excessive decomposition of fat.

Of all the endocrine glands other than the pancreas, the thyroid exercises the most significant control over metabolism. Hyperthyroidism is nearly always associated with an increased metabolism, emaciation, and a lowered carbohydrate tolerance. Occasionally sugar appears in the urine on a mixed diet, and epinephrin glycosuria is easily induced. The combination of Graves' disease and diabetes has been occasionally described, but in this association the diabetes runs its course independently of variations in the thyroid symptoms. Feeding thyroid to normal individuals or animals reduces sugar tolerance and occasionally leads to spontaneous glycosuria.

In myxedema, the carbohydrate metabolism factors are the

reverse of those in Graves' disease   The basal metabolism is reduced, sugar tolerance is increased, and an accumulation of fat is strikingly characteristic   The tendency to epinephrin glyco-suria is markedly reduced

It must not be inferred that all instances of derangement of thyroid function fall regularly as regards sugar tolerance into one of these two groups   Such an inference would be opposed to all our clinical experience with disease of the thyroid gland It is well known how irregularly the symptoms of abnormal thyroid function are grouped   Sometimes autonomic symptoms predominate, sometimes sympathicotonic, sometimes the two vary in different domains, hyperthyroidism may be followed by hypothyroidism or the reverse, and not infrequently symptoms of hyper- and hypothyroidism are conjoined   This variation explains why sometimes a clinical picture of predominating hyper-thyroidism is associated with increased sugar tolerance, why an increased tolerance may be replaced by decreased tolerance, or vice versa, and how in rare instances diabetes is associated with outspoken symptoms of myxedema   Falta, who, as I have previously stated, regards the action of the thyroid as op-posed to the pancreas function, believes that much of the ir-regularity that exists depends upon the functional range of the pancreas   If the range be wide, the thyroid will influence car-bohydrate tolerance but little, whereas, if it be small, the thyroid influence will easily be asserted

The experimental work of Cushing has shown the intimate relation between hypophysis function and glycosuria and obesity As is well known, the pituitary body consists of two separate ds which are distinct embryologically, histologically, and physiologically   The anterior portion or pituitary gland is developed from the epithelium of the buccal cavity, the posterior portion or hypophysis from cells of the central nervous system The pituitary exercises a marked influence upon growth and de-velopment, but apparently only the hypophysis is concerned in carbohydrate metabolism   However, it has long been known that overfunction of the pituitary is frequently associated with overfunction of the hypophysis, and the association of acro-

megaly and diabetes was commented upon by Marie   Borchardt collected 176 cases of acromegaly from the literature, and found diabetes to be present in 63, and in 8 more alimentary glycosuria had been noted   Sometimes the diabetes is of a severe type and leads to death, but more often it is of a mild form, and there may be lack of correspondence between carbohydrate ingestion and sugar excretion

The relation of sugar tolerance to disease of the hypophysis shows great variation, just as it does in relation to disease of the thyroid   As a rule, when other distinct symptoms of hyper-pituitarism are present, the tolerance is low, when other symptoms point definitely to hypopituitarism, it is high   But as symptoms of acromegaly frequently culminate in a clinical picture of hypopituitarism, so glycosuria may be replaced ultimately by a high sugar tolerance, and during the transition stages the carbohydrate relation may vary from time to time The absence of a constant relation between carbohydrate metabolism and hypophyseal disease, for instance, a high sugar tolerance associated with acromegalic features, has proved an unsolvable puzzle to many clinicians   Indeed, Allen, largely upon this basis, denies the hypophysis any specific control over carbohydrate metabolism   However, that such apparent contradictions should exist must appear quite reasonable

The only clinical complex associated with deficiency of the adrenals is Addison's disease   In this condition the blood-sugar is usually low, epinephrin glycosuria is absent, and sugar tolerance is high.   Emaciation is the rule, but this is probably the result of the digestive disturbances rather than of deranged metabolism.   The interpretation of the clinical symptoms of Addison's disease is complicated by the complex structure of the adrenal glands   The cortex is interrenal tissue derived from the mesothelial cells of the genital ridge, the medulla is chromaffin tissue derived from the nervous system   While there is reason to believe that the chromaffin tissue furnishes the secretion that influences the carbohydrate metabolism, it is probable that the cortex is responsible for some of the symptoms of Addison's disease

Conditions of hyperfunction of the chromaffin tissue have no sound clinical foundation   The attempt to associate the hypertension of nephritis with hyperepinephrinemia have not been successful   Instances of true adrenal diabetes are unknown

From what has been said thus far you must see that glycosuria is not peculiar to diabetes, that it is not fair to conclude that every patient with sugar in the urine has diabetes   Sugar in small amounts may be found in the urine in a variety of conditions, and it often requires very careful investigation before one can make a definite decision   Since reduction tests are almost exclusively used to detect sugar in the urine, we must first of all be sure when only slight reduction occurs that the reaction is due to sugar and not to some other substance   We must further determine that the glycosuria is associated with hyperglycemia and is not due to abnormal renal permeability   Finally, if indeed the condition be a genuine hyperglycemic glycosuria, we must by careful clinical study decide whether the condition be due to mild diabetes or to disturbed function of one or more of the ductless glands, for instance, to thyroid or hypophyseal disease   I hesitate to comment upon so trite a matter as the proper directions to give patients when asking for specimens of urine, and I should not do so were I not convinced by experience of the tremendous importance of this apparently trivial matter   If you ask patients for a specimen of urine, almost invariably will they bring a portion of the urine passed upon arising   From the standpoint of detecting a small amount of sugar this is the least desirable specimen of the twenty-four hours   In the early stages of diabetes and in mild forms of the disease glycosuria occurs only transiently after meals   The best specimen to examine is the urine passed from two to four hours after the largest meal of the day   It is important, therefore, as a routine, to instruct all patients to send two specimens of urine, one from the night voiding passed a few hours after dinner, the other from the early morning voiding   I have known of mild cases of diabetes overlooked in spite of repeated urine examinations because the specimen examined was always from the morning voiding, and each year I detect 5 or 6 mild cases of diabetes with sugar

in the evening specimen and none in the morning. Besides the question of discovering glycosuria, the routine practice of examining morning and evening specimens has other advantages. The evening specimen often contains a little albumin and a few casts when the morning specimen contains neither, and in cases of nephritis the two specimens frequently show such a wide difference of specific gravity that an important estimate of renal function is at once obtained.

For the practising physician the readiest and most satisfactory test to confirm the presence of sugar when there is slight reduction is the fermentation test, and this additional evidence should never be neglected. If the reduction be due to sugar, we must proceed further and determine the relation of the blood sugar to the glycosuria. We have proposed a relatively simple test to determine this that gives a quicker and more satisfactory insight into the carbohydrate metabolism of a patient than any other method with which I am familiar. The test consists in studying the fasting blood sugar and the blood sugar and urine one-half hour, one hour, and two hours after administering 100 grams of glucose. I cannot go into details of the test, briefly, in normal persons the blood-sugar mounts only a little, and soon returns to the fasting level, whereas, in diabetes the blood-sugar goes much higher and the rise is longer sustained. In normal persons sugar appears in the urine if the blood sugar reaches 0.18 per cent. Mild forms of renal diabetes are frequently disclosed by this method, and it is important to distinguish these from mild forms of diabetes.

In the few remaining minutes I must compress my *remarks* upon one of the most important aspects of carbohydrate metabolism, one well deserving a much more extended consideration. I have already emphasized the fact that although *fat is built up* largely from sugar, this process is apparently not *reversible* some evidence points distinctly against fat being a source sugar. Glycerin is certainly converted into sugar, *but the* acids are not. All fatty acids found in the human body is even number of carbon atoms, and since *the*
occurs always at the next to the last carbon atom,

splitting has proceeded far enough, a molecule of β oxybutyric acid is formed   I have already pointed out that those amino-acids which are not converted into sugar are easily converted into β-oxybutyric acid   This acid body, therefore, comes both from protein and from fat, but by far the larger amount comes from fat   The tremendous disturbance of fat metabolism in severe diabetes is often indicated by the large amount of fat in the blood   It would appear that the need for carbohydrate is so great that the transportation of fat from the subcutaneous depots is stimulated far beyond the capacity of the organ or organs concerned in its burning   It must not be thought that protein and fat metabolism follow abnormal channels in diabetes, all the evidence is against this view   However, in some curious and unknown way the satisfactory burning of β-oxybutyric acid requires the concomitant burning of sugar   In starvation, aceto-acetic acid and acetone rapidly appear in the urine, to disappear promptly upon the administration of carbohydrate   In diabetes, these acid bodies, instead of being burned, frequently accumulate in the body, upset the acid-base equilibrium, and cause the serious and dangerous group of symptoms known as acidosis

A fundamental requisite for the proper transaction of meta-bolic affairs is a fine adjustment of the reaction of the body juices   The reaction may vary only within a small margin, and since acids are taken into the body in great excess of bases, the body must possess an efficient machinery to maintain a constant reaction   Bases must be present to neutralize acids as rapidly as they are formed, and there must be a way of eliminating acids while bases are retained, or the supply of base would soon be exhausted   When the supply of base is exhausted a fatal in-toxication occurs

The body possesses an admirable machinery to meet these demands   There are three ways in which it protects itself against an overwhelming accumulation of acid

1 The blood is so constituted that a large amount of acid or alkali may be added to it without changing the re-action

2 A large amount of acid is eliminated through the lungs and kidneys

3 A large amount of the ammonia formed in the body may be used to neutralize acid

As Henderson and Palmer have pointed out, the blood represents a remarkably suitable mixture to maintain a constant reaction. Owing to the ready adjustment between the proportion of carbonates and bicarbonates and between the proportion of mono- and dibasic phosphates, large amounts of acid or alkali may be absorbed without altering the reaction   The proteins also may absorb a considerable amount of acid without changing reaction.

The lungs excrete large amounts of carbon dioxid   In the lung, carbon dioxid is given off from the carbonates which are returned to the tissues as bicarbonates, which there absorb carbon dioxid and return again to the lungs as carbonate   If the amount of acid in the blood rises, this free play between carbonate and bicarbonate is interfered with   Much of the bicarbonate is removed to hold the acid, so that carbon dioxid accumulates in the tissues and in the blood, the carbon dioxid tension in the lungs falls, and the stimulation of the respiratory center by the retained carbon dioxid produces increased ventilation of the lungs in an effort to restore the balance

The kidneys have the very remarkable power to separate an acid secretion from a faintly alkaline mixture, and in this way a large amount of acid is excreted from the body while valuable alkali is retained

Finally, a large amount of ammonia is formed in the body from the decomposition of protein   Normally, most of this ammonia combines with carbon dioxid to form urea, but in the presence of an excess of acid much of it may be diverted to neutralize this acid, which is then excreted by the kidney as an ammonium salt.

We now possess numerous clinical methods to detect when the acid equilibrium mechanism of the body is disturbed, when it is being taxed, and when it is approaching exhaustion   The stage of exhaustion is readily appreciated by the profound alteration

in the character of the respiration known as air hunger, and serious manifestations of intoxication by the nervous system, chiefly coma. But long before these dangerous symptoms arise, relatively innocent changes point to a warning. In diabetes, abnormal acid bodies may be present in the urine as the earliest indication of an excessive acid accumulation, and an important object in treatment is to control metabolism so that these bodies are permanently absent from the urine. A decrease of bicarbonate in the blood may be measured either directly or in terms of the carbon dioxid tension in the alveolar air. The total alkali reserve of the body may be approximated by measuring the bicarbonate tolerance. The ammonia diversion may be measured by estimating the ammonia nitrogen in the urine. Finally, the reaction of the blood may be discovered by determining the hydrogen-ion concentration of the dialysate and its so-called buffer value.

For practical purposes the two methods usually employed are to examine the urine for aceto-acetic acid and acetone and to follow the carbon dioxid tension in the alveolar air. These two methods yield the greatest amount of information for the least outlay of time and skill. If a third is to be added, the estimation of the ammonia nitrogen in the urine is to be recommended.

L G , age fourteen, male, black, single

The patient entered the hospital on December 13, 1918, complaining of swelling of the stomach.

Family History —Unimportant

Past History —The boy's general health has been good, though he has never been robust. Whooping-cough at five years and measles at seven years the only infections No history of cough Appetite and digestion good

Present Illness —About December 1st the patient began to feel drowsy and tired, and to sit in the house instead of running out and playing with the other boys He became steadily worse, and a few days later his mother noticed that his abdomen was swelling Since then his condition has grown progressively worse. He feels chilly in the evening and has fever, and the abdomen has steadily increased in size

Physical Examination —Temperature 101° F Pulse 136 Respirations 44 Blood pressure 110/80 The patient is markedly underdeveloped and undernourished Respirations are rapid. Slight unproductive cough Mentally dull Examination of the head showed no noteworthy abnormality No glandular enlargement. *Lungs* The lower borders have a high position and in the left axilla a friction rub is heard The heart shows no abnormality *Abdomen* Greatly distended Skin is shiny and tense Small umbilical hernia Marked fluid wave and shifting dulness General tenderness

Laboratory Findings —*Blood* Hb 70 per cent. R B C 5,664,000 W B C 7400 Differential count essentially normal. *Urine* Essentially normal. *Stools* Show no abnormality Wassermann negative

On December 14, 1918, 4 liters of clear, serous fluid were removed from the abdomen After tapping the spleen was palpable, the abdominal wall was still held tensely, and there

was resistance in the right lower quadrant, but no mass could be made out   The x-ray report December 17th, 1918, shows pleural thickening at left base, with high position of the diaphragm on both sides

Course in Hospital —After admission to the hospital the patient continued to run a high, irregular fever   The leukocytes have remained in the neighborhood of 8000   The abdominal swelling has decreased somewhat   The patient has lost weight and has become very emaciated   On January 8, 1919, a friction-rub was noted in the lower right axilla   On March 12th a large pleural effusion was discovered on the right side   The von Pirquet tuberculin test is positive

Mr ——— has given the history of this patient, and the situation presents no diagnostic difficulty   The colored boy has been in the hospital about two months, and during his residence here has shown this irregular fever, with rapid pulse   The abdomen now is not very prominent, it is a little tender and quite tense, but there is no muscle spasm   There is a small amount of free fluid   Here between the costal margin and the umbilicus is an indefinite transverse mass   These abdominal symptoms were present on admission, although they have changed somewhat, that is, the amount of fluid has lessened and the resistance in the epigastrium has gradually developed   During his stay in the hospital a pleural friction-rub was observed on the left side, and later on the right side   The boy now has a marked pleural effusion on the left side, as is well shown in these x-ray plates

The diagnosis of tuberculous peritonitis is not always as easy as it is in this case, although the diagnosis is usually not so difficult in children as in adults   For practical purposes it is convenient to divide tuberculous peritonitis into the ascitic and the dry forms   In children the ascitic form, when accompanied by fever, offers no obstacles to diagnosis   The only conditions with which it might be confused are—

1 Certain unusual instances in emaciated infants when fluid in the intestines is mistaken for fluid in the peritoneal cavity

2 Thrombosis of portal vein. The condition is not common and the history usually distinguishes it.

3 In the older literature much is written about an idiopathic form of peritonitis that comes on insidiously in adolescence particularly in girls With slight or no constitutional symptoms a peritoneal effusion gradually develops which lasts a short time and then slowly disappears All such cases that have been operated upon were shown to be tuberculous, and it is only reasonable to assume that they are tuberculous

In adults the diagnosis of the ascitic form is further complicated by its resemblance to cirrhosis of the liver and carcinomatosis of the peritoneum Even at operation the differentiation between carcinoma and tuberculosis of the peritoneum may remain in doubt until microscopic examination of sections of an excised nodule decides the difficulty During the past winter you have seen cases in the wards where it was impossible to decide definitely between the three conditions Where there are in addition to ascites marked constitutional symptoms, and abdominal tenderness and pain, the diagnosis is usually clear If, in addition to the peritoneal manifestations, there are also signs of pleural or pericardial involvement, the diagnosis is certain. In doubtful cases, the presence of a definite tuberculous focus elsewhere, for instance, in the lungs or testicles, may establish the diagnosis The differentiation of tuberculous peritonitis from cirrhosis of the liver is especially difficult because the two conditions are so frequently associated In the terminal stages of cirrhosis, tuberculous peritonitis is often added.

In the dry form of tuberculous peritonitis the diagnosis is beset with greater difficulties When the symptoms come on acutely they may be mistaken for appendicitis or cholecystitis The hospital records of the surgical side show many instances operated upon under such mistaken impressions Four or five patients have been operated upon for intestinal obstruction, and tuberculous peritonitis quite unexpectedly discovered at operation In still another group operated upon for hernia the peritoneum was found studded with tubercles, sometimes the hernial sac alone being involved

Of special interest are the curious abdominal tumors that are often found and which not infrequently mislead   These tumors are formed—

1 By the rolled-up omentum
2 By encapsulated fluid
3 By matted intestines
4 By enlarged glands
5 By pelvic masses

The commonest abdominal tumor is the rolled-up omentum It forms a characteristic boggy, ill-defined mass stretching transversely across the abdomen a little above the umbilicus Encapsulated fluid may simulate a cyst, and this error in diagnosis has frequently been made   Spencer Wells operated upon a patient for ovarian cyst   The condition was found to be an encapsulated tuberculous exudate, and the patient recovered so satisfactorily and unexpectedly that operation was advised for tuberculous peritonitis, and this method of treatment has remained popular to this day   Coiled intestines form indefinite boggy masses that are quite characteristic   They are often multiple   Sometimes the whole small intestine is coiled up as an adherent mass in the region of the umbilicus   Tumors formed of enlarged retroperitoneal and mesenteric glands are rarely encountered in adults   Even in children they are uncommon   Pelvic masses, strictly speaking, should not be included in peritoneal tumors   However, I do include them on account of their frequent occurrence and their importance The usual sequence of events is that a diagnosis of pelvic inflammatory disease is made, the patient is operated upon, and unexpectedly the peritoneum is found studded with tubercles, the pelvic mass is found also to be tuberculous and is removed, the patient makes a satisfactory and a complete recovery   It is just these cases that have given such great prestige to the operative treatment of tuberculous peritonitis

In considering tuberculous peritonitis I wish to view the condition from three different angles

1 As a local tuberculous disease, just as one speaks of pulmonary tuberculosis as a local tuberculous disease

2 As one manifestation of the whole course of tuberculous infection

3 As a part of a disease affecting the large serous cavities

Of tuberculous peritonitis as a local disease I may say that it is a very serious and grave tuberculous manifestation   In this respect it contrasts markedly with tuberculous pleurisy, which is one of the mildest tuberculous manifestations   It occurs more commonly in children than in adults, but the difference in this respect is not extreme   I have already spoken of the general clinical features and the diagnosis of the condition   The prognosis is always grave, although many cases and even some very severe and complicated cases recover   Some years ago I investigated the subsequent history of all the patients with tuberculous peritonitis who had been in the hospital   The immediate results are as follows

Discharged from the hospital as well	16 cases.
Discharged improved	71
Discharged unimproved	15
Died	48 "

This gives an immediate mortality of 32 per cent in all cases. The gynecologists had by far the best record—only 5 deaths in 48 cases, or 10 per cent.

An effort was made to discover the subsequent results in the patients leaving the hospital   All were written to and those living in the city were personally hunted up and visited. From Dr Bloodgood I obtained the after results in a number of the surgical cases   In all, 43 cases were heard from   Of these

14 were reported dead	33 per cent
7 were reported living, but not well	16 "
22 were reported living and quite well	51

Of the 14 cases reported dead,

3 died within three months.
1 died within one year
3 died within two years.
1 died after one year from acute intestinal obstruction.
1 died after three years from carcinoma
1 died after two years from an operation said to have gall-stones.

Of the 7 living, but not well,

> 1 was living after ten years Feels strong and well, but sinus
>   persists
> 1 was living after six years, but has tuberculous glands in the
>   neck
> 1 was living after six years, has attacks of abdominal pain,
>   but is otherwise well
> 1 was living after six years, writes that she is thin and weak.
> 1 was living after four years with a persisting sinus
> 1 was living after two years with a persisting sinus
> 1 was living after one year, but with a swollen abdomen and
>   enlarged liver

Of the 22 living and well,

2 cases living and well after ten				years
1 case	"	"	"	" eight	"
2 cases	"	"	"	" seven	"
1 case	"	"	"	" six	"
1 case	"	"	"	" five	"
2 cases	"	"	"	" four	"
6 cases	"	"	"	" three	"
4 cases	"	"	"	" two	"
3 cases	"	"	"	" one year	

Tuberculous peritonitis is then a very fatal disease, and even when there is improvement, the after-results are not very brilliant Still, one can never say what the outcome will be in a given case, and some of the least promising turn out the best One of the cases that recovered had, besides the peritonitis, pleurisy with effusion, pneumothorax, and tubercle bacilli in the ~~" tum~~

The only point in the treatment of tuberculous peritonitis that deserves special consideration is the question of operation You will find if you investigate the matter that opinion is divided And, indeed, it has always appeared to me that the question of the value of operation cannot possibly be settled on the basis of the data at present available The statistics that have been published are very unsatisfactory Those who advocate operation admit that only selected cases are suitable for operation, and the cases they select happen to be the very cases that

do best under medical treatment   How unreasonable to compare results obtained on selected cases with results obtained on all cases   Cases of tuberculous peritonitis accidentally discovered at operation are nearly always very mild cases, indeed, many of them never give symptoms   These two are included among surgical cases   I must say that I am not enthusiastic about operation, for I feel that no satisfactory proof of the value of operation has been offered   The only group of physicians who get good results in the treatment of tuberculous peritonitis are the gynecologists   In their cases the tuberculous pelvic disease is the important thing, the tuberculous peritonitis, which is often local, is incidental.   When the large pelvic tuberculous masses are removed the tuberculous peritonitis heals readily

Before speaking of tuberculous peritonitis as a manifestation of tuberculous infection in the individual and of tuberculous peritonitis as a part of a general serous membrane disease, I wish to show the second patient

R. G , age fourteen, male, black, single

The patient entered the Johns Hopkins Hospital on February 17th, complaining of pain around the heart.

Family History —Gives no details of interest.

Past History —The patient has always been healthy up to onset of present illness   He has suffered from many attacks of sore throat.   As a child he had pneumonia   He thinks he has lost some weight

Present Illness —One month before admission to the hospital the patient noticed pain over the heart and shortness of breath   The pain became worse, but the shortness of breath did not increase   There was loss of appetite, some nausea, and on one occasion vomiting   The pain gradually became so bad that one week ago the patient was obliged to leave school and go to bed   For the past week he has had a sweat each night   He has noticed no particular loss of strength

Physical Examination —Temperature 100 4° F   Pulse 04   Respirations 22.   Blood pressure 114/70   Fairly well nourished colored boy, a little apathetic   Mucous membranes pale,

Large, scarred tonsils, with large glands at angle of jaw Fairly marked general glandular enlargement, including epitrochlears *Heart* Slight wavy precordial impulse The area of cardiac dulness is increased, it extends 4 cm to the right and 16 cm. to the left of the median line The area of dulness extends upward in a triangular shape The heart sounds are clear, but distant. Loud to-and-fro friction to the left of the sternum *Lungs* At the left base there is a little impairment and distant breath sounds due to pulmonary compression *Abdomen* Shows no noteworthy abnormality

Laboratory Findings—*Blood* Hb 60 per cent R B C 4,420,000 W B C 9400 The differential count is essentially normal Wassermann reaction negative *Stool* negative

Course in Hospital—During the patient's stay in the hospital he has run an irregular fever and a rapid pulse The temperature has gradually diminished and it is now normal The pulse-rate has continued to be rapid The friction rub has disappeared and the area of cardiac flatness has decreased in size The signs of compression of the left lower lobe have disappeared

As you see, the patient had on admission this high, irregular fever, which has gradually come down to normal His pulse rate too has fallen There is still a wide area of cardiac flatness, but there has never been an extensive effusion You see here in the x-ray that the heart shadow has not the characteristic triangular form extending up to the neck which is an indication of pericardial effusion The cardiohepatic angle is well preserved and when the effusion is small this angle is not always obliterated To contrast with this picture we have here another of a patient who was in the hospital a year ago You see this tremendous shadow filling up nearly all of the lower part of the chest and tapering up to the sternal notch This is the largest pericardial effusion I have ever seen In the instance of the patient we show today there was never any occasion to consider aspirating the pericardium The heart action was not embarrassed by the small amount of fluid present Although it has the appearance of being very simple, you must not believe that

it is always easy to drain the pericardium, even though a large effusion be present. The patient with this extreme effusion was aspirated twice, and on each occasion only about 500 c c. could be withdrawn. You have seen the shaggy exudate on the pericardial surfaces in pericarditis, and it is very difficult to keep the lumen of the needle clear. I have seen other cases where tapping was unsuccessful, and the suggestion has been made that it would be well in such cases to introduce a small, soft rubber catheter into the pericardial sac. Large pericardial effusions requiring aspiration do not occur frequently. But it is important that you be familiar with the details of the operation. *A propos* of an interesting case, Dr Thayer discusses the matter fully in an article that appeared in the Bulletin a few years ago.

The diagnosis in this instance is so obvious that it requires no discussion. I have already said that tuberculous peritonitis is much less common than tuberculous pleurisy, and tuberculous pericarditis is much less common than peritonitis. The cause of this disproportion depends, no doubt, upon the different incidence of tuberculous disease in the organs which these serous sacs cover or lie contiguous to. Tuberculosis affects the lungs more commonly than any other organ, tuberculosis of the liver, spleen, and intestines occurs much less frequently, tuberculosis of the heart is a great rarity. I do not mean to imply that tuberculosis of a serous surface is always directly spread from an underlying lesion in an organ. We are, unfortunately, very poorly informed about the mode of invasion in serous membrane tuberculosis. In the peritoneum it may be spread from a tuberculous lesion in the intestines, in the pelvis, or in the abdominal lymph-glands. When such a direct spread cannot be demonstrated, we must assume invasion through the lymph channels or through the blood-stream. The lymph currents flow always away from the serous surface, and to make this route plausible we must assume retrograde infection, always an unsatisfactory assumption. Nor does the blood-stream offer an easier explanation. It is difficult to see how the vessels to the peritoneum alone become infected, and in instances where the disease is local and not a part of a generalized tuberculosis,

the infection of the blood-stream could not occur at a distant point In tuberculous pericarditis the infection comes nearly always from a contiguous mediastinal gland A very remarkable case was demonstrated last year in which tuberculosis in the mediastinal glands had involved the pericardium and the heart muscle, and a caseous focus had finally ruptured directly into the cavity of the heart

Tuberculous pericarditis stands between pleurisy and peritonitis as regards prognosis It is a more serious manifestation than pleurisy, less serious than peritonitis

We come now to view serous membrane tuberculosis as one manifestation of the course of tuberculous infection Tubercle bacilli, after they enter the body, are carried rapidly to the lymph-glands Dr Krause has shown, in an interesting series of experiments, that it is almost impossible to directly infect the lungs Provided a thorough emulsion of tubercle bacilli be used, large numbers may be injected directly into the ear vein and none can be recovered from the lungs They must, of course, lodge there, but with great rapidity they are transported to the bronchial lymph-nodes Most of them are filtered out in this way, but the filter is by no means perfect Dr Krause has further shown that if guinea-pigs be inoculated into the groin, the inguinal glands quickly become infected, but a few days after the inoculation the bronchial glands are also infected Organisms must enter the blood-stream, be carried to the lungs, and from there be transferred to the bronchial glands If infection be slight, perhaps only the regional glands are infected, but in many instances a wide glandular infection oc-

After such a primary infection has occurred the behavior of the animal toward subsequent infections is promptly altered All of the cells of the body become so sensitive to the tubercle bacillus and its products that they react violently when brought in contact with it Koch observed this reaction and describes it clearly I will read you his description

"When one inoculates a healthy guinea-pig with a pure culture of tubercle bacilli the wound as a rule, closes and in the first days seems to heal However, in from ten to fourteen

days a hard nodule appears which soon breaks down, leaving an ulcer that persists to the time of the death of the animal There is quite a different sequence of events when a tuberculous guinea-pig is inoculated   For this experiment animals are best suited that have been successfully infected four to six weeks previously   In such an animal the inoculation wound likewise promptly unites   However, no nodule forms, but on the next or second day after a peculiar change occurs   The point of inoculation and the tissues, about over an area of from 0 1 to 1 cm in diameter, grow hard and take on a dark discoloration. Observation on subsequent days makes it more and more apparent that the altered skin is necrotic. It is finally cast off and a shallow ulceration remains which usually heals quickly and permanently without the neighboring lymph-glands becoming infected."

This reaction is now generally described as a hypersensitive reaction, and it is important to be familiar with its manifestations, for without such knowledge it is impossible to have a clear understanding of the clinical manifestations of tuberculosis

An animal infected with tuberculosis rapidly acquires an altered power of reaction toward subsequent injections of tubercle bacilli. This altered reactivity is exhibited in different ways, depending upon the manner and the intensity of the reinfection

1. If a large number of tubercle bacilli are injected, the animal dies in a few hours with symptoms of a profound intoxication.

2. If the dose be small, there is a prompt reaction about the site of injection which destroys the tubercle bacilli and prevents infection even of the regional lymph-glands

3 If the size of the dose be larger than that which the animal is able to resist, but not large enough to liberate acute fatal intoxication, infection does occur, but the resulting lesions are chronic and slowly progressing as compared with those produced by the same dose in normal controls

These results, so contradictory at first sight, are easily

the infection of the blood-stream could not occur at a distant point In tuberculous pericarditis the infection comes nearly always from a contiguous mediastinal gland A very remarkable case was demonstrated last year in which tuberculosis in the mediastinal glands had involved the pericardium and the heart muscle, and a caseous focus had finally ruptured directly into the cavity of the heart

Tuberculous pericarditis stands between pleurisy and peritonitis as regards prognosis It is a more serious manifestation than pleurisy, less serious than peritonitis

We come now to view serous membrane tuberculosis as one manifestation of the course of tuberculous infection Tubercle bacilli, after they enter the body, are carried rapidly to the lymph-glands Dr Krause has shown, in an interesting series of experiments, that it is almost impossible to directly infect the lungs Provided a thorough emulsion of tubercle bacilli be used, large numbers may be injected directly into the ear vein and none can be recovered from the lungs They must, of course, lodge there, but with great rapidity they are transported to the bronchial lymph-nodes Most of them are filtered out in this way, but the filter is by no means perfect Dr Krause has further shown that if guinea-pigs be inoculated into the groin, the inguinal glands quickly become infected, but a few days after the inoculation the bronchial glands are also infected Organisms must enter the blood-stream, be carried to the lungs, and from there be transferred to the bronchial glands If infection be slight, perhaps only the regional glands are infected, but in many instances a wide glandular infection occurs After such a primary infection has occurred the behavior of the animal toward subsequent infections is promptly altered All of the cells of the body become so sensitive to the tubercle bacillus and its products that they react violently when brought in contact with it Koch observed this reaction and describes it clearly I will read you his description

"When one inoculates a healthy guinea-pig with a pure culture of tubercle bacilli the wound, as a rule, closes and in the first days seems to heal However, in from ten to fourteen

days a hard nodule appears which soon breaks down, leaving an ulcer that persists to the time of the death of the animal There is quite a different sequence of events when a tuberculous guinea pig is inoculated For this experiment animals are best suited that have been successfully infected four to six weeks previously In such an animal the inoculation wound likewise promptly unites However, no nodule forms, but on the next or second day after a peculiar change occurs The point of inoculation and the tissues, about over an area of from 0 1 to 1 cm in diameter, grow hard and take on a dark discoloration. Observation on subsequent days makes it more and more apparent that the altered skin is necrotic. It is finally cast off and a shallow ulceration remains which usually heals quickly and permanently without the neighboring lymph-glands becoming infected."

This reaction is now generally described as a hypersensitive reaction, and it is important to be familiar with its manifestations, for without such knowledge it is impossible to have a clear understanding of the clinical manifestations of tuberculosis.

An animal infected with tuberculosis rapidly acquires an altered power of reaction toward subsequent injections of tubercle bacilli. This altered reactivity is exhibited in different ways, depending upon the manner and the intensity of the reinjection

1 If a large number of tubercle bacilli are injected, the animal dies in a few hours with symptoms of a profound intoxication.

2. If the dose be small, there is a prompt reaction about the site of injection which destroys the tubercle bacilli and prevents infection even of the regional lymph glands

3 If the size of the dose be larger than that which the animal is able to resist, but not large enough to liberate acute fatal intoxication, infection does occur, but the resulting lesions are chronic and slowly progressing as compared with those produced by the same dose in normal controls

These results, so contradictory at first sight, are easily

the infection of the blood-stream could not occur at a distant point   In tuberculous pericarditis the infection comes nearly always from a contiguous mediastinal gland   A very remarkable case was demonstrated last year in which tuberculosis in the mediastinal glands had involved the pericardium and the heart muscle, and a caseous focus had finally ruptured directly into the cavity of the heart

Tuberculous pericarditis stands between pleurisy and peritonitis as regards prognosis   It is a more serious manifestation than pleurisy, less serious than peritonitis

We come now to view serous membrane tuberculosis as one manifestation of the course of tuberculous infection   Tubercle bacilli, after they enter the body, are carried rapidly to the lymph-glands   Dr Krause has shown, in an interesting series of experiments, that it is almost impossible to directly infect the lungs   Provided a thorough emulsion of tubercle bacilli be used, large numbers may be injected directly into the ear vein and none can be recovered from the lungs   They must, of course, lodge there, but with great rapidity they are transported to the bronchial lymph-nodes   Most of them are filtered out in this way, but the filter is by no means perfect   Dr Krause has further shown that if guinea-pigs be inoculated into the groin, the inguinal glands quickly become infected, but a few days after the inoculation the bronchial glands are also infected   Organisms must enter the blood-stream, be carried to the lungs, and from there be transferred to the bronchial glands   If infection be slight, perhaps only the regional glands are infected, but in many instances a wide glandular infection occurs   After such a primary infection has occurred the behavior of the animal toward subsequent infections is promptly altered   All of the cells of the body become so sensitive to the tubercle bacillus and its products that they react violently when brought in contact with it   Koch observed this reaction and describes it clearly   I will read you his description

"When one inoculates a healthy guinea-pig with a pure culture of tubercle bacilli the wound, as a rule, closes and in the first days seems to heal   However, in from ten to fourteen

days a hard nodule appears which soon breaks down, leaving an ulcer that persists to the time of the death of the animal There is quite a different sequence of events when a tuberculous guinea pig is inoculated. For this experiment animals are best suited that have been successfully infected four to six weeks previously In such an animal the inoculation wound likewise promptly unites However, no nodule forms, but on the next or second day after a peculiar change occurs The point of inoculation and the tissues, about over an area of from 0 1 to 1 cm in diameter, grow hard and take on a dark discoloration Observation on subsequent days makes it more and more apparent that the altered skin is necrotic It is finally cast off and a shallow ulceration remains which usually heals quickly and permanently without the neighboring lymph-glands becoming infected "

This reaction is now generally described as a hypersensitive reaction, and it is important to be familiar with its manifestations, for without such knowledge it is impossible to have a clear understanding of the clinical manifestations of tuberculosis

An animal infected with tuberculosis rapidly acquires an altered power of reaction toward subsequent injections of tubercle bacilli This altered reactivity is exhibited in different ways, depending upon the manner and the intensity of the reinfection

1 If a large number of tubercle bacilli are injected, the animal dies in a few hours with symptoms of a profound intoxication

2 If the dose be small, there is a prompt reaction about the site of injection which destroys the tubercle bacilli and prevents infection even of the regional lymph-glands

3 If the size of the dose be larger than that which the animal is able to resist, but not large enough to liberate acute fatal intoxication, infection does occur, but the resulting lesions are chronic and slowly progressing as compared with those produced by the same dose in normal controls

These results, so contradictory at first sight, are easily

reconcilable   It is reasonably probable that the mechanism, whatever it may be, which causes the immediate toxic reaction on reinfection is the same upon which the animal withstanding this reaction depends for its complete protection   How analogous these phenomena are to the general principles of anaphylaxis is at once apparent   The animals have by one infection been rendered hypersensitive to subsequent contact   This hypersensitiveness is a valuable protective asset, but if the reinfecting dose be large the animal succumbs with the symptoms of an acute intoxication

Dr Trudeau, in his experiments on immunity to tuberculosis, has found that the more virulent the organism, the higher is the degree of protection against reinfection   In his experiments, histologic examination of the organs showed a remarkable difference in the type of reaction   The tuberculous animals showed upon reinfection an early and violent inflammatory reaction about the bacilli, which was followed in many cases by disintegration of the bacilli and subsequent absorption of the exudate   In normal animals no such immediate inflammatory reaction occurs about the injected tubercle bacilli   Tubercles slowly form and then go on to caseation

Infection of the serous sacs shows the same relations that have been described for the general infection of animals   In uninfected animals little or no reaction is occasioned by the injection of tubercle bacilli, and the organisms are rapidly transported to the neighboring lymph-glands   In infected animals an immediate and violent inflammatory reaction is produced, followed by extensive exudation   Masses of shaggy exudate cover the surface and serous fluid accumulates in the sac

Serous membrane tuberculosis is, therefore, a local hypersensitive reaction to infection in an already infected person   Only on this basis can we explain the acute onset of symptoms, the fibrous exudate, and the serous effusion   It illustrates also how a relatively small infection may cause a wide-spread and violent reaction   It is possible that a subserous focus of disease may cause serositis without tubercle bacilli actually reaching the surface   The infrequency with which tubercle bacilli can be

demonstrated in the serous effusion of serous membrane tuberculosis lends some support to such a possibility

I come finally to the last consideration, that is, to view tuberculous peritonitis and tuberculous pericarditis as a part of disease of the large serous sacs I have already commented upon the great frequency with which more than one serous cavity is affected This combination is often enough observed clinically, anatomically it is still more striking Some years ago I analyzed the autopsy records of 35 cases of tuberculous peritonitis and discovered these remarkable relations

Twelve cases had an associated peritoneal and pleural tuberculosis and 9 more showed pleural adhesions without demonstrable tubercles.

In 2 cases there was an associated peritoneal and pericardial tuberculosis, and in 1 more an adherent pericardium without demonstrable tubercles.

One case showed tuberculosis of all three serous membranes.

Two cases had adherent pleuræ and pericardium without demonstrable tubercles.

In 1 case there was peritoneal and pleural tuberculosis with adherent pericardium in which no tubercles were found.

Direct channels of communication between the serous cavities have not been demonstrated, but our clinical experience inclines us to assume their presence

Tuberculous polyserositis has a close relation to an interesting group of cases exhibiting a chronic inflammation of one or more of the serous sacs These cases are described in the literature as Zuckergussleber (Curschmann), pericarditic pseudocirrhosis (Pick), polyserositis, and polyorrhomenitis They are characterized by—

1 A chronic inflammation with the formation of a dense, thick, fibrous exudate

2 Transient attacks of acute inflammation

3 The formation of abundant effusions

4 The absence of bacteria and of typical histologic structure in the fibrous exudate

5 The striking chronicity of the condition

The relation of this type of chronic inflammation of the serous membranes to tuberculosis has been widely discussed

Some cases clinically identical with chronic polyorrhomenitis are proved at autopsy to be tuberculous, some cases not definitely tuberculous harbor foci of tuberculosis in the organs or glands, in the majority of cases there is no distinct evidence of tuberculous disease This disease and its relation to tuberculosis is fully discussed by Kelly and by Nicolls

BIBLIOGRAPHY

Hamman, L The Statistics of Tuberculous Peritonitis from the Clinical Records of the Johns Hopkins Hospital, Johns Hopkins Hosp Bull, xix, No 210, September, 1908

Paterson Pleural Reaction to Inoculation with Tubercle Bacilli in Vaccinated Normal Guinea-pigs, American Review of Tuberculosis, 1917, i, 353

Rist, Kindberg, and Rolland Etudes sur la réinfection tuberculeuse, Ann. de méd , 1914, i, 310–375

Krause Attempts to Alter Cellular or Tissue Immunity to Tuberculosis and Its Relation to the Pathology of Tuberculosis, Tr Natl Assn for the Study and Prevention of Tuberculosis, p 243

Hamman and Wolman Tuberculin in Diagnosis and Treatment, 1912

Thayer Observations on Two Cases of Tuberculous Pericarditis with Effusion, Johns Hopkins Hosp. Bull , Baltimore, 1904, xv, 149–155

Kelly, A. O J Multiple Serositis, Tr College of Physicians, Philadelphia, 1902, xxiv, 62

Nicolls On a Somewhat Rare Form of Chronic Inflammation of the Serous Membranes, Studies from the Royal Victoria Hospital, Montreal, 1902, i, 147

AURICULAR FIBRILLATION

S R., age forty five, female, white, widow

Entered the hospital November 14, 1918 complaining of shortness of breath and swelling of legs   The patient has been under observation in the Out-patient Department since 1909 She has had three previous admissions to the hospital, the first in April, 1916, the second in November, 1916, the third in October, 1917   A diagnosis of mitral stenosis and insufficiency was made when she came to the Out patient Department in July, 1909   This diagnosis has been confirmed on all subsequent ad missions to the hospital   When she was in the hospital in April, 1915, the pulse was irregular and the electrocardiographic study demonstrated typical auricular fibrillation   On the second admission in November, 1916, the Wassermann reaction was positive   On each occasion the patient has entered the hospital with the characteristic symptoms of myocardial in sufficiency   On her first admission it was also noted that the pupils were irregular and that they failed to react to light

Family History —Shows nothing of importance

Past History —Numerous attacks of tonsillitis in childhood, but no history of rheumatism   Panhysterectomy performed in 1905 for pelvic abscess   The patient has had shortness of breath on exertion for at least twenty years   For ten years there has been cough with occasional bloody expectoration. Some swelling of the legs during the past year

Present Illness —Five weeks before admission to the hospital she began to have marked palpitation of the heart, and shortness of breath again became extreme   Two weeks before, her legs began to swell and she experienced precordial distress

Physical Examination —Temperature 98 6° F   Pulse 96 Respirations 36   Blood pressure 138/90   Patient is poorly de veloped and emaciated, marked dyspnea and orthopnea   Legs moderately edematous   Lips and cheeks cyanosed   Has con

siderable cough, with mucoid expectoration   Typical Argyll
Robertson pupils, a little irregular   Dental caries and oral
sepsis

Lungs   Fluid in the right pleural cavity, numerous moist
râles

Heart   Extremely enlarged, the area of superficial dulness
measuring 6 cm to the right and $17\frac{1}{2}$ cm to the left of the median
line   At the apex, a rough diastolic murmur, snapping first
sound and loud, blowing systolic murmur   Second pulmonic
sound accentuated   Pulse totally irregular—small volume
Ventricular venous pulse   *Abdomen* Distended   Slight hernia
in scar of operation wound   Moderate ascites   Liver extends to
the umbilicus   Spleen not enlarged   Deep reflexes normally
active

Laboratory Notes —Blood   Hb 92 per cent   R B C
4,664,000   W B C 5720   Differential count essentially nor
mal   *Urine* contains a moderate amount of albumin and numer
ous hyaline and granular casts   *Wassermann* reaction negative.

Electrocardiographic Report (November 18, 1918) —Rate 80
Rhythm totally irregular   No P-waves present   T-wave
negative in Lead 2   Diagnosis Auricular fibrillation, right
ventricular preponderance

Course in Hospital —During patient's stay in the hospital
her symptoms have improved

Diagnosis —Chronic rheumatic endocarditis, mitral stenosis,
auricular fibrillation, myocardial insufficiency, syphilis, cere-
brospinal syphilis

F C , age thirty-two, male, colored, single
Came into the hospital November 7, 1918, complaining of
shortness of breath, cough, and abdominal discomfort   The pa-
tient had been in the hospital from August 3, 1918, to Septem-
ber 5, 1918   At that admission the diagnosis of chronic endo-
carditis, mitral insufficiency, and myocardial insufficiency was
made   On the first admission the patient entered the hospital
for shortness of breath   The family history was essentially
negative   The patient stated that his general health had been

good up to the onset of the symptoms that brought him to the hospital There was a definite history of rheumatic fever in 1913 In the winter of 1917 he had an attack of pleurisy Four years previously he had had a chancre, and he received treatment for only three weeks After leaving the hospital he was admitted again on October 1, 1918, and discharged on October 27th. On this occasion he came in again for shortness of breath On both admissions the patient responded satisfactorily to treatment and was discharged from the hospital improved After his discharge on October 27th the patient was able to walk several blocks without discomfort

Present Illness —On November 1st he caught cold and soon after became very short of breath and had abdominal discomfort Cough developed and he had mucoserous expectoration His throat has been a little sore The patient thinks he has had no fever The shortness of breath became so marked that he has been obliged to sit propped up in bed His legs have become swollen, but not so markedly as on the previous admissions His appetite has been very poor and he has vomited frequently The patient has had abdominal discomfort, described as "heaviness," and a dull pain in the abdomen particularly when he gets up He has been sleeping poorly at night.

Physical Examination —Temperature 98 6° F Pulse 108 Respirations 26 Blood pressure 158/112 Fairly well nourished Marked dyspnea and orthopnea. Slight pitting of legs and ankles. Examination of the head showed no noteworthy abnormality except the dental caries and oral sepsis *Lungs* Showed only the signs of pulmonary congestion, with a small amount of fluid at the right base *Heart* Was enlarged, the area of relative cardiac dulness measuring 5 cm to the right and 11 cm to the left of the median line Rhythm regular, except for an occasional extrasystole A loud, blowing systolic murmur at the apex and markedly accentuated second pulmonic sound *Abdomen* Showed a small amount of ascites and a large, tender liver

Laboratory Notes —*Blood* Hb 70 per cent R B C. 5,600,000 W B C 7680 Differential count essentially nor-

mal The Wassermann reaction, which had been positive on the two previous admissions, was doubtfully positive *Urine* Contained a moderate amount of albumin and a small number of casts

Course in Hospital —Under digitalis therapy the patient's condition improved The pulse-rate, which on admission was 120, fell to 54 A definite bigeminal rhythm developed, which was broken by irregular groups of extrasystoles On November 9th an electrocardiographic study showed a complete auriculo-ventricular dissociation, with varying auricular and ventricular rhythm, and an occasional ventricular response When digitalis was stopped, the ventricular rate remained low, but the auricles began to fibrillate On November 13th the electrocardiographic study showed "Rate 60 per minute Rhythm totally irregular No P-waves T-wave inverted and almost imperceptible in all three leads " As the pulse-rate increased the rhythm again became regular At the same time the patient, whose general condition had improved, became very short of breath, the liver became greatly swollen and pulsated Electrocardiographic report on November 20th reads as follows "Rate 120 Rhythm regular P-R interval 0 14 second Ventricular deflection quadriphasic in Lead III and of low voltage T-wave in Lead III practically iso-electric Slight left ventricular preponderance " On November 21st the patient received 0 5 mg of strophanthin, and the same dose on the two succeeding days The pulse-rate fell to 65 The patient became comfortable and the swollen liver gradually went down to normal size The rhythm remained regular except for occasional extrasystoles On November 27th the following electrocardiographic report was made "Rate 58 Rhythm regular P-R interval 0 2 second T-waves all positive " Since that date the patient's condition has remained unchanged

E K , age fifty-four, male, white, married
The patient entered the hospital on November 7, 1918, complaining of heart trouble He has had three previous admissions to the hospital The first admission was in August, 1917, when

a diagnosis of myocardial insufficiency, auricular fibrillation, and colloid goiter was made   The patient left the hospital on September 14, 1917, improved   He was admitted to the hospital again for shortness of breath on November 30, 1917, when the same diagnosis was made   After leaving the hospital he was better for a while, but in June, 1918, the symptoms recurred, and he was admitted again, leaving the hospital improved on July 13th.

Family History —Contains nothing of importance

Past History —The patient has always been strong and healthy up to onset of present illness   He has had a goiter for at least forty years   Although this has grown to a considerable size, it has never given him any discomfort

Present Illness —The patient's illness began in August, 1917, when he was obliged to stop work on account of shortness of breath, weakness, and swelling of the legs   These symptoms have recurred persistently since then. After the patient's discharge from the hospital on July 13, 1918, he returned to his work as a policeman and was well until October 31st, when severe shortness of breath again came on. He was obliged to stop work on November 4th, and since then has had marked dyspnea and orthopnea

Physical Examination —Temperature 98° F   Pulse 84   Respirations 34   Blood pressure 158/104   The patient is fairly well nourished   Marked dyspnea and orthopnea   Edema of legs and the dependent parts   Lips cyanotic   The examination of the head shows nothing important except oral sepsis   The thyroid is greatly enlarged, the right lobe larger than the left, the whole gland is very irregular and firm.   *Lungs*   Show no important abnormality except for the presence of fluid in the right pleural cavity   *Heart*   Is enlarged, the area of cardiac dulness extending 5 cm to right and 16 cm to left of median line   No murmurs   Aortic second sound somewhat accentuated   The pulse is totally irregular, there is a slight pulse deficit, the radials are slightly thickened   *Abdomen*   Liver a little below costal margin

Laboratory Findings —Examination of the blood showed no

important abnormality The Wassermann reaction was negative Phthalein test 79 per cent excretion in two hours Adrenalin test was quite negative

Electrocardiographic Report (November 11, 1918)—Rate 80 Rhythm irregular P-wave absent One right ventricular premature beat T-wave inverted and ventricular complex diphasic in all three leads Low voltage in all three leads, especially in Leads I and II, with notching of the initial deflection Impression Auricular fibrillation and ventricular extrasystole

Course in Hospital—During his stay in the hospital the patient has shown marked improvement under digitalis therapy The shortness of breath and the edema have completely disappeared

F W, age fifty-one, male, white, married

The patient entered the hospital November 16, 1918, complaining of shortness of breath and swelling of abdomen and legs

Family History—Essentially negative

Past History—Had been a healthy man up to onset of the present illness There is a history of morning cough for the past ten or fifteen years, and cough at night as well for the past six or seven years He has used tobacco and alcohol moderately, otherwise nothing noteworthy in the past history

Present Illness—In the summer of 1916 the patient began to have shortness of breath on exertion and indefinite pain in the abdomen His legs and body became swollen Under treatment his condition improved At the end of December, 1916, he had another attack of shortness of breath, abdominal pain, and edema Ever since then he has had shortness of breath and some swelling of the legs, which, however, has varied a good deal in intensity from time to time One year ago he was confined to bed for seven weeks on account of these symptoms Since then he has been obliged to spend two or three weeks in bed on different occasions He has been on a low diet for the past two years, and he attributes his weakness and loss of weight to this He has lost about 40 pounds Nycturia three to four times during the past year He has become very nervous and irritable.

These 4 patients presenting different clinical pictures have all certain features in common For instance, they all show the clinical manifestations of myocardial insufficiency Likewise, they all have an irregular pulse It is this irregular pulse so similar in type in the 4 patients with clinical manifestations in other respects so dissimilar that I wish to consider especially this morning

Here is a patient with mitral stenosis who has had symptoms on the part of the heart for over twenty years, for nine or ten years her pulse has shown always, at least whenever she has been examined, the same kind of irregularity that is present this morning

As you feel the pulse you notice at once that the beats come at irregular intervals and are of varying amplitude The pulse is slow—about 70 beats to the minute—and although one does not get at the first touch the sensation of extreme irregularity that one gets when under the same conditions the pulse beats rapidly, still, one has a better opportunity to study the condition in detail If the pulse is felt carefully, you note that no two beats are separated by the same interval, hardly any two beats have the same force As you listen over the heart and feel the pulse, you notice that some contractions are too feeble to be registered at the wrist If you put on the blood-pressure cuff, the variation in force of the beats is still more strikingly shown

As you look at the vein in the neck, instead of the double undulation and the systolic emptying of the veins ordinarily seen, there is but a single pulsation, and this comes synchronously with ventricular systole

The second patient has mitral insufficiency, the result of rheumatic endocarditis The pulse at present is perfectly regular, but you have heard the history

While the patient was under observation in the ward the heart action suddenly became very irregular At the end of about twenty-four hours the normal rhythm returned Shortly after the onset of the irregularity breathlessness increased, the liver ..lly swelled and became a pulsating mass, again rapidly de- ..g in size after the irregularity ceased In this instance

the irregularity of the heart action seems to have been the immediate cause of the break in cardiac compensation.

The next patient has an enlarged thyroid, and associated with it a greatly enlarged heart. Although a systolic murmur is heard, there is the best of grounds for believing that he has no valvular lesion I cannot stop to consider the relation between the enlarged thyroid and the heart condition, but there is a mass of clinical observations that justify our belief that there is a very intimate relation between the two In this patient the myocardial insufficiency in the absence of valvular disease and hypertension and pulmonary disease is certainly the result of extensive myocardial disease When the patient first came to the hospital about eighteen months ago his heart was very rapid and extremely irregular If I remember clearly the history of this first admission, the rapid, irregular heart action and the symptoms of myocardial insufficiency came on together Under treatment the pulse quieted down, the irregularity became less marked, and the symptoms of myocardial insufficiency disappeared Since then the pulse has remained slow, but quite irregular, the condition that now persists

Finally, in the fourth case with a complicated clinical picture which we will not stop to consider in detail, we again find this same peculiar and interesting irregularity of the heart action The heart is beating slowly, but, as in the other cases, the beats come at irregular intervals and are of unequal force This patient has hypertension, and no doubt the hypertension together with myocardial changes explains the myocardial insufficiency Which of these two factors plays the more important part it is impossible to say

To all of us older physicians who have practised medicine for twenty years or more this remarkable irregular heart action holds a fascinating interest. We have lived through the period when the nature and meaning of this phenomenon were totally obscure, then through the period when in spite of better methods of observation it still eluded discovery although shrewd surmises were being made about it, and finally, through the crowning period, when with still better methods the mystery was solved

The story of the development of our knowledge of this form of cardiac irregularity is one of the most interesting and useful chapters in modern medicine   I shall tell you the story briefly

I remember seeing these cases as a student and an intern No special comment was made upon them except the platitudinous note that the pulse was irregular in force and rhythm   Not infrequently, however, the clinical picture was more dramatic and called for stronger terms   Patients came into the hospital breathless, with swollen legs and enlarged, tender liver, the heart beat tumultuously without rhyme or rhythm in almost a convulsive frenzy.   The condition was then dignified with the term "delirium cordis"   It was noticed that this delirium cordis occurred with noteworthy frequency in mitral stenosis and it was often referred to as the mitral pulse   When it occurred in mitral stenosis it was clearly noted that certain interesting changes occurred in the heart sounds   The presystolic murmur became changed in time and character and frequently disappeared altogether   The booming first sound, however, persisted, and on the character of this sound and the associated clinical findings adepts would confidently make a diagnosis of mitral stenosis, to the surprise and admiration of tyros   One more clinical symptom was frequently observed in these patients   The veins in the neck, which often stood out prominently, failed to show the normal venous undulation, in its place a prominent systolic pulsation was seen which was attributed to tricuspid insufficiency

In those days the only graphic records made were of the radial pulse   I doubt if any of you has ever seen a Dudgeon syphmograph, but it was a familiar instrument on the wards at that time The radial tracing showed just what could be felt at the wrist, and I remember that we were more interested in a scrutiny of the character of the pulse-wave than we were in fruitlessly trying to analyze an obvious irregularity

In 1902 a very remarkable book appeared entitled "Study of the Pulse," by Mackenzie   You all no doubt know that Mackenzie was at that time a general practitioner in a relatively small

ory He has since become one of the foremost clinical authorities upon the heart

Mackenzie before 1890 began using jugular as well as radial tracings in the study of the heart's action Such observations had been made previously by Riegel, for instance, but he was the first to use the method systematically

Before the publication of his book in 1902 definite progress had been made in the recognition of cardiac irregularities Extrasystoles were fully understood, and nearly all the important facts concerning heart-block had been worked out However, this curious irregularity which we are now discussing remained entirely unexplained Let me read you what Mackenzie says of his own observations

"My attention was first directed to this condition as a separate and definite entity about 1890 I had been endeavoring to discriminate between the different forms of irregular heart action, and it occurred to me to employ the jugular pulse as an aid By this means I was able to separate the great majority of irregularities into definite groups, according to the mechanism of their production, as revealed by simultaneous records of the jugular and radial pulses. There was one group which showed a distinct difference from all others, by the presence of the ventricular form of the venous pulse I was at a loss to understand the nature of the heart's action in these cases, and as I found them very frequently among people with a history of rheumatism, I determined to watch individual cases with rheumatic hearts, to see when this irregularity arose, and when the auricular venous pulse changed to the ventricular The individual recorded as Case 48 came under my care in 1880, suffering from an attack of rheumatic fever I examined her at intervals until her death in 1898 Up to 1897 her heart was regular, except for occasional ventricular extrasystoles Her jugular and liver pulses were always of the auricular form There was a well marked presystolic murmur She became very ill in 1897, with a rapid and irregular heart. When the heart slowed down after a partial recovery, I found that the jugular and liver pulses were of the ventricular form, that the presystolic murmur had disappeared,

and that the heart was irregular, in other words, all evidences of auricular activity had disappeared   From this date onward I was able to confirm these observations, and add to them other cases which showed waves due to the auricle, in jugular and apex tracings before the heart became irregular, and their disappearance when the heart became irregular   Thus, I established that all the positive evidences of auricular activity capable of being revealed by clinical methods showed the cessation of auricular action with the onset of this irregularity   For many years I speculated as to the cause of auricular fibrillation   As the auricle was found distended and thin-walled at the postmortem examination, I came to the conclusion that the disappearance of the signs of auricular systole was due to the auricle having become distended, atrophied, and paralyzed "

What a remarkable statement that is, and what a simple and still penetrating deduction from his observations   Had Mackenzie only stopped there!   Unfortunately, further observations led him off from this simple and sound conclusion and landed him at last in gross error   Let me continue with Mackenzie's own words

"Shortly after this was published I had a series of cases, some of which I had watched for years, and at the postmortem examinations the auricles were not thinned, but were hypertrophied   With this fact before me I saw that my previous explanation could not be correct, for the fact that the auricles were hypertrophied indicated that they must have contracted during the years that I had watched them, and when there had been an absence of all signs of auricular activity   As it was clear that the auricles could not have contracted during the normal period—that is to say, immediately before ventricular systole —the only alternative I could see was that they contracted during ventricular systole   As, in the meantime, I had studied several hundreds of cases and had seen this condition start under a variety of circumstances, particularly in individuals with frequent extrasystoles, I put forward the view that ventricles and auricles contracted together, and assumed that the stimulus for contraction arose in some place that affected auricles and

ventricles simultaneously As at this time I could not conceive of any other possibility to explain the facts, I suggested that the stimulus for contraction arose in the auriculoventricular node, and I called the condition 'nodal rhythm.' "

While Mackenzie was pursuing his work in England, clinicians in other countries were busy with similar methods of investigation I may mention particularly Wenckebach in Holland and Herring in Germany All other known forms of cardiac irregularity were soon accurately analyzed and their mechanism understood, but the most interesting and striking of all the irregularities remained unexplained It refused to fit itself into any of the known categories, all one could say of it was that it was an unanalyzable irregularity which when once begun nearly always persisted Almost in despair, clinicians called it the irregularly irregular pulse, the absolutely irregular pulse, the pulsus irregularis perpetuus

In 1906 a fresh shaft of light was shot into the obscurity, this time by a laboratory worker Cushny was at that time Professor of Pharmacology at Ann Arbor, and he published his observations in conjunction with Edmunds. The article is so important that I shall read a few short excerpts from it

"The following case of marked irregularity of the heart occurred in the service of Dr Peterson, Professor of Gynecology and Obstetrics in the University of Michigan Careful examination of the heart was made and a number of sphygmographic tracings were obtained Unfortunately, at that time we were not acquainted with Mackenzie's methods of taking the venous and liver pulses, and failed to take advantage of this most valuable method of analyzing cardiac irregularity The case is of considerable interest, however, and the light which seems to be thrown on it by our experience of irregularity in animal experiments encourages us to put it on record In the course of the long series of experiments and demonstrations on the dog's heart carried out in the pharmacological laboratory of the University of Michigan during the last seven years it has happened occasionally that on opening the chest the heart was found to be beating very rapidly and irregularly Doubtless other

workers in this field may have had similar unfortunate experiences, but we are unaware of any recorded cases. Our dogs were anesthetized with morphin, 0 2 to 0 3 gram hypodermically, and chloretone administered by the stomach-tube. The operation consisted in performing tracheotomy, prolonging the median incision to the lower end of the sternum, sawing through the sternum along its whole length, and hooking the two sides of the chest apart, thus exposing the pericardium, which was opened. The myocardiograph was then applied to the ventricle and auricle and tracings taken on a kymograph with smoked paper. The anesthesia was invariably deep enough to prevent any manifestation of pain and the eyelid reflex was absent before the incision was made. Sometimes, however, spontaneous respiratory movements returned while the sternum was being cut through, or if these were present before, they became quickened and deepened. It was soon noted that when this change occurred the tendency to cardiac irregularity was much greater than in those experiments in which more profound anesthesia had been induced. Attempts were made to record the changes in the pulse during the operation, but in the experiments in which this was done the irregularity was not developed. In several cases, however, it was noted that the heart rhythm was normal before and during the first part of the operation, but that when respiratory movements were induced by cutting through the sternum, the pulse, which had previously been of the usual slow vagus type seen in the dog, suddenly became accelerated and irregular. On examination of the heart in these cases, before the apparatus was applied to it, the ventricles were found in rapid, irregular movement, the relaxation was often very imperfect between three or four successive contractions, and then more complete for one or two beats. The impression was given that the ventricles were responding to a series of very rapid impulses which prevented their diastole, and that they could only relax when their irritability was reduced by fatigue, and then the more complete diastole followed. The auricles were widely dilated and no systole occurred in them, they were not wholly paralyzed and inactive, however, for on close inspection the fibers proved to

be in a stage of continual inco-ordinated contraction, each part of the auricle undergoing continuous fibrillary contraction independent of all other parts. The heart was, in fact, in the condition known to physiologists as auricular delirium, or fibrillary contraction in the auricle. Of course, we cannot claim to have shown any connection between this type of irregularity in the dog's heart and that in the case described. At the same time there exist similarities between them, and the sudden arrest of the irregularity in each suggests a common cause, in the dog the site of the lesion is the central nervous system, and the history of the patient suggests that here also the irregularity was of central origin. We had hoped to have the opportunity of continuing the investigation in other cases of irregular heart, but as circumstances preclude our working further together, we have decided to put the imperfect investigation on record, in the hope that others may be interested in the suggestions made and may be able to prove or disprove its correctness.''

Cushny carried these observations to a number of clinicians, among others to Mackenzie and Wenckebach. In his conversation with Cushny, Mackenzie showed tracings displaying small, rapid waves upon the venous pulse tracings, and both agreed that these might be the effects of auricular fibrillation. Indeed, Mackenzie the following year published such tracings, but he thought the condition transient and of little practical consequence. Certainly he failed to appreciate its real significance. Wenckebach replied to Mackenzie that such slight waves upon the venous pulse tracing were sometimes seen in tracings from hearts beating regularly. He was unwilling to allow that auricular fibrillation could be at the bottom of an irregularity lasting for years.

I must digress a moment to prepare you for the next development in this interesting story. Physiologists had long before noted that as muscular tissue contracts interesting electric changes occur in the muscle mass, namely, the contracting portion becomes electrically negative and currents flash through the muscle. In 1887 Waller was able to register the electric currents passing through the heart muscle by connecting the limbs

with a capillary electrometer   The instrument, however, was clumsy, and did not record accurately enough to be used as a clinical method   In 1903 Einthoven published his discovery of an unusually delicate galvanometer   By suspending a very delicate thread of silvered quartz in a magnetic field he was able to register deflections caused by the very faintest electric currents   In 1907 clinical reports of results obtained by using this instrument to register the heart action currents began to appear, and in 1909 Lewis, in England, and Rothberger and Winterberg, in Germany, by using this method established beyond question that the totally irregular heart action in man and experimental auricular fibrillation in dogs are identical

We are indebted to instruments of precision and to all this painstaking work for the elucidation of the mechanism of the cardiac irregularity illustrated in these patients and which we now know to be due to auricular fibrillation   However, once this condition is fully understood, it is easily diagnosed by rough clinical methods   No physician can give as an excuse for lack of familiarity with auricluar fibrillation that an electrocardiograph is not available or that he is unable to devote sufficient time to obtain satisfactory polygraphic tracings   During the past five years we have made it a rule to diagnose all cardiac irregularities on the ward before electrocardiograms are taken   It is only occasionally that auricular fibrillation is missed   We meet auricular fibrillation in two forms   fibrillation with rapid pulse and fibrillation with slow pulse   With the onset of fibrillation the ventricle nearly always beats very rapidly and very irregularly, under treatment the ventricle slows down and the irregularity becomes much less marked   Fibrillation with rapid pulse is very easily recognized, when the ventricle beats slowly the pulse may on casual observation appear to be regular, but even under these conditions the diagnosis can be made in most instances by more careful observation   The conditions under which there is real difficulty in diagnosis are few   If there is complete auriculoventricular block, the fibrillating auricle has no influence over the ventricle   The pulse is slow and regular and the condition of the auricles would scarcely

therefore, is less than the ventricular rate counted over the heart   The pulse deficit is greater when the ventricle is beating rapidly than when it is beating slowly, and usually when the ventricle rate is below 60 no deficit occurs

4 In fibrillation, the more rapid the pulse, the greater the irregularity   This is in marked contrast to extrasystolic and sinus arhythmias, where the converse is true   Exercise often brings out this distinction

5 If a venous pulse can be made out in the neck, it is of the so-called ventricular type   That is, but a single large wave is observed which is systolic in time

Clinically, auricular fibrillation is observed under the most varied conditions, it occurs in hearts already diseased, but also in hearts that present no evidence of any abnormality whatsoever aside from the fibrillation   It occurs with noteworthy frequency when the auricles are subjected to great distention, and is, therefore, commonly associated with mitral ste nosis   But it occurs very often in connection with other valvular defects, in hearts hypertrophied from long-continued hypertension or from obstruction in the pulmonary circulation and in myocardial disease of every type   Of peculiar interest is the occurrence of fibrillation in hearts that present no other evidence of disease   The fibrillation comes on usually in paroxysms quite similar to the paroxysms of paroxysmal tachycardia   Such attacks may occur for many years, but in the end the fibrillation usually remains permanently   When hearts that are diseased begin to fibrillate, the fibrillation commonly persists during the remaining lifetime of the patient   This is peculiarly true in mitral stenosis   However, in conditions other than mitral stenosis, and particularly in myocardial disease, brief periods of fibrillation are commonly observed   I am becoming more and more impressed by the frequency with which transient periods of fibrillation occur in old people   After sixty, fibrillation may come on with varied upsets which have no direct connection with the heart   Gastro-intestinal disturbances frequently inaugurate it   As the symptoms of the acute disturbance pass off, fibrillation also disappears   I have seen 2 patients have such transient

attacks of fibrillation over a period of years and the fibrillation finally become permanent

What I wish particularly to impress upon you is that you must look upon auricular fibrillation as an independent and distinct clinical entity, I mean independent of the particular cardiac disease with which it may happen to be associated, and as distinct from manifestations of myocardial insufficiency   Auricular fibrillation occurs frequently enough in otherwise normal hearts where it is the whole of the clinical picture, and when it occurs in hearts already diseased it adds something new and distinct to the clinical picture   Rather than to look upon it as one sign of a failing heart muscle, it were better to view it, which in fact it commonly is, as an important cause of myocardial insufficiency   A normal heart may stand auricular fibrillation without the slightest evidence of impaired function, but when the heart is handicapped by mechanical disadvantages, or its muscle is diseased, then the advent of fibrillation is quite commonly the added difficulty with which it cannot contend, and the usual symptoms of myocardial insufficiency are precipitated   How frequently does just that occur in mitral stenosis   With the onset of fibrillation the balance is upset and breathlessness and edema rapidly come on, under proper treatment the ventricles slow down, abortive, fruitless contractions are eliminated, the circulatory balance is re-established, and the symptoms of myocardial insufficiency disappear   The auricles continue to fibrillate with slow ventricular rate, and fibrillation may thus continue for many years.

I have emphasized the importance of regarding auricular fibrillation as a distinct clinical entity, and this emphasis is peculiarly warranted in speaking of treatment   Aside from any of the conditions with which it may be associated, fibrillation has a special, and I may almost say a specific, treatment.   A normal heart subject to transient attacks of fibrillation may need no treatment, but if the paroxysm be prolonged the efficiency of the heart will suffer, as it nearly always does when fibrillation occurs in a diseased heart   We possess no remedy that will stop fibrillation and re-establish normal auricular movements, but we

can inhibit the fruitless agitation of the ventricles that fibril
lation induces   It is in fibrillation that digitalis exercises its
wonderful power   When the heart is brought under satisfac-
tory digitalis influence the ventricular rate is slowed and with
the slowing its action becomes more regular and the individual
beats more effective   And digitalis must be given until this
quieting effect is obtained or evidence of poisoning occurs
Only occasionally is a fibrillating heart refractory to digitalis
Time does not permit me to speak at length of the use of digi
talis and its mode of action   I can only add one warning
Since the potency of digitalis preparations varies tremendously,
it is futile to prescribe digitalis according to routine dosage   A
teaspoonful of one infusion, for instance, may be as potent as a
tablespoonful of another   Unfortunately, most preparations on
the market are not standardized, and it is important that the
physician should prescribe a preparation according to its effects
and not according to text-book dosage   If an accurately stand-
ardized preparation is not obtainable, then the physician should
use a single preparation with which he has become familiar   Its
effect upon fibrillating hearts will be an index of its potency   You
cannot write a prescription for tincture of digitalis for 6 patients
if each patient has the prescription filled at a different druggist,
and expect the same effect in all

BIBLIOGRAPHY

Potain   Bull et mém Soc méd d hôp de Paris, May, 1867
Mackenzie   Study of the Pulse, 1902
Wenckebach   Die Arhythmie, etc , 1903
Cushny and Edmunds   Amer Jour Med Sci , 1906, cxxxiii, 66
Mackenzie   Diseases of the Heart, 1913, 3d edition
Lewis   Mechanism of the Heart beat, 1911
Wenckebach   Die Unregelmässige Herztatigkeit, 1914
Hoffmann   Elektrographie als untersuchungsmethode, etc., 1914

CLINIC OF DR. ALLEN K KRAUSE

JOHNS HOPKINS HOSPITAL

A CASE OF MULTIPLE TUBERCULOSIS IN CHILDHOOD

Full and Complete History of the Patient from His First Appearance at the Clinic in this Hospital Ten Years Previously, Onset of the Disease, the Influence of Trauma on the Production of Both Bone and Joint Tuberculosis, Site of First Infection, the Etiology of the Infection, Progression of Infection and Disease, Treatment, Full Discussion of the Use of Tuberculin, Sanatorium and Home Treatment, The Pirquet Skin Test; Prognosis

January 15, 1919

PRESENTATION OF THE CASE

THIS boy, born in the United States, of Italian parentage, is within a few weeks of his fourteenth birthday He is 53 inches tall and weighs 70 pounds, yet well proportioned, with clear eye and good color, and every appearance of health His physique, therefore, is that of a normal ten year-old child To account for his size we may at first think of his race, yet his brother whom you see here with him is almost two years younger, though a full half head taller and weighing 93 pounds

He has been under almost continuous observation at this hospital for ten years, and with this appearance of vigor and ruddiness before you let us review his story

On January 27, 1909, he was brought to the dispensary, referred to the Dermatological Clinic, and from there at once transferred to the Surgical Clinic He had a sore arm Twenty five days before he had fallen and struck his left arm and hand on the floor Several days later the forearm became swollen and very painful At about the same time his legs began to swell, and

this swelling persisted   Pain that was more severe at night had been constant in his arm and both legs   On the nineteenth day of his disease the swelling on his arm had been opened by a physician, and at the time of the patient's first visit to the dispensary this wound was still open and was discharging

He was then just completing his third year   He was the fourth of five children   One brother and two sisters were living and in good health   One sister had died at the age of one year of what the mother said was "mumps"   His father, forty years old, and his mother, thirty-four, were both well

From birth he had always been healthy   He had escaped the infectious diseases of infancy and childhood   He had never before been ill

He showed the rosary, sabre shins, and epiphyseal enlargements of rickets that had been recovered from   There was a small sinus over the left ulna at about the junction of the lower and middle thirds   The overlying skin was tender and inflamed, and evidently covered an abscess   Pressure in this region caused pus to exude   There was no bony thickening that could be felt. Over both tibiæ there was also slight tenderness and possibly slight swelling, though the latter was very difficult to make out.

The boy entered the hospital a week later, where on February 4th he was operated on   Through a small incision over the left ulna, at the site of the abscess, a small amount of pus was evacuated and the bone exposed   Though the sinus went down to the periosteum, no bare bone was felt   The ulna, explored to the marrow cavity, was found to be perfectly normal

The patient left the hospital on February 13th with his wound granulating well, with no pain or discomfort, and with instructions to return in two days to the dispensary for dressings After a few days, however, it was noticeable that he was not doing so well   He now began to complain more about his right leg, and whereas a month before it had been noted that "there was possibly slight swelling" over the tibiæ, though this "was very difficult to make out," on February 27th we find the record of "a smooth even swelling on the right shin bone, painful to pressure, apparently bone involvement, periostitis"   By March 10th decided

fluctuation had developed, the tenderness was great, and the child looked quite ill. Meanwhile pus had again begun to exude from the unhealed operation wound in his left forearm

He was therefore again sent into the hospital for operation on his right leg. On March 12th an incision was made over the most prominent part of the tibial swelling and the abscess explored. The abscess cavity was found to be inside the tibia. There was a small defect in the periosteum which was considerably roughened and thickened. At the same time the left arm was again gone into, when a pus cavity and a periosteal and bony defect of the radius was found. On March 22d the boy left the hospital with both wounds clean, the discharge slight, and granulations healthy and abundant.

From this time until the fall of 1909 the patient came regularly to the dispensary to have his wounds dressed. A diagnosis of syphilitic periostitis and epiphysitis was made, and, in addition to the local applications of boric ointment, a course of therapy with mercury and potassium iodid was instituted. Both of these measures continued for seven months when on October 30, 1909, we have a note that the arm was healed, the ulcer on the leg about healed, and the patient discharged with a dry gauze dressing on his leg. Antisyphilitic treatment was, however, continued during the following winter, though up to this time there is no record of a Wassermann test having been performed.

On February 21, 1910, or thirteen months after he first came under observation, the child again returned to the Surgical Dispensary after an absence of two months this time with a new complaint. He "comes in today with an enlarged left epitrochlear gland and also enlarged right inguinal glands, all quite tender and temperature over them elevated, although the skin is not red." He was given treatment with potassium iodid, and, since no change in his condition occurred, on March 5th he was transferred to the Pediatrics Clinic.

He here came under the observation of Professor Pirquet and from the notes then made we begin to gather a few more pertinent details of history that are not to be found in the earlier records. We find that the sister who died of "mumps" at the

age of one year was a twin sister   The patient did have an infectious disease earlier in childhood   He had had measles when two years old   At the sites of his operation scars there is still some tenderness   For a month now his mother had noticed a swelling in his right groin, and for the last fifteen days a similar swelling on the inner side of his left elbow   His mouth is in poor condition   His throat and neck are negative   His heart and lungs are negative   His abdomen, however, is greatly distended, though symmetrically so   In the region of the descending colon there are masses to be felt.   The edge of the liver is palpable 2 cm below the costal margin   The spleen is not palpable   He was given a Pirquet skin test with old tuberculin and reacted strongly

We have then in March, 1910, a five-year-old boy, born and brought up in a family in which there is no history of tuberculosis, whose twin sister died of "mumps" at the age of one year, who had rickets in infancy and measles at two years, who when almost four years old and in apparent health fell and injured his arm, as a consequence of which a lesion of his left ulna and radius developed   At the same time his legs are noticed to be swollen and an abscess of his right tibia gradually comes to light   Diagnosed as luetic epiphysitis, these bone abscesses are operated on, but heal with great sluggishness After a year the lymph-nodes that drain the areas that first show disease begin to exhibit manifest involvement   And now a simple test—the Pirquet skin test—is applied, and it is found that the case is probably one of tuberculosis   Physical examination reveals no involvement of the neck or lungs, but does bring out unususal abdominal distention and palpable masses in the abdomen along the descending colon   The points to which we would call attention for the moment are (1) the development of a chronic bone lesion following injury, (2) the subsequent manifestation of another bone lesion at a remote focus, (3) the swelling of the legs that was recorded at first admission, but to which apparently no further attention was paid, (4) the involvement of neighboring lymph-nodes that took a full year to become manifest, (5) the hint thrown out that there is

some intra abdominal trouble, (6) the normal pulmonary findings, and (7) the errors of omission in the handling of the case, such as incomplete history taking and the failure to make early Wassermann and Pirquet tests. At any rate, at the end of a year we are practically certain that we have here in a young child manifest tuberculous adenitis of two widely separated lymphnodes that has originated from unrecognized tuberculosis of bones with the bony involvement not yet completely healed (there is still tenderness), and there is a suggestion that all is not right in the abdomen.

From the Pediatrics Department the child was transferred to the Phipps Tuberculosis Dispensary, and here he became a patient on March 8, 1910 Under our observation during the nine years that have since elapsed we have had an unusual opportunity to note carefully the periodic arrest of disease, the halting march of manifest tuberculosis from point to point, the development and effects of other acute infections, the immediate and remote results of various therapeutic measures, the fluctuations of constitutional conditions, such as weight and temperature, and the variations of tolerance to tuberculin During these first five years, from 1910 to 1915, we saw him from once to several times weekly, from 1915 to 1917, usually twice a month, and since January, 1918, at longer and more irregular intervals This boy's history would furnish an almost complete epitome of the more common and characteristic manifestations of tuberculosis in early life, and from it many texts might be drawn and enlarged upon It will be possible to take up with any attempt at detail only a few, most can be only alluded to or touched upon briefly And before discussing any broader features of his case, we may rapidly sketch what has happened to him since he was known to be a case of tuberculosis

His original history at the Tuberculosis Dispensary, taken on March 8, 1910, mentions that he has no cough, no pain, and no gastro-intestinal irregularities except for a very poor appetite He has night sweats, and for four months his feet have been swollen His weight is 35 pounds, a deficiency of about 6 pounds for his age His skin and mucous membranes are pale

His temperature in the clinic is 99° F , his pulse 120, and his respirations 26   He comes complaining of large but painless swellings of the epitrochlear and inguinal glands and abdominal distention   More complete examination makes certain that his lungs are normal to percussion and auscultation, while his liver is palpable

Tuberculin therapy was at once begun, and on March 12th he was given $\frac{1}{100000}$ mgm old tuberculin subcutaneously   Two days later his back was slightly red and swollen and sore to the touch at the point of injection   Every few days he received tuberculin, and by March 29th had reached $\frac{4}{100000}$ mgm   Two days later the area about the point of injection is much swollen, very red, and very tender   In other words, at the very beginning of treatment he exhibits an extremely high degree of hypersensitiveness to tuberculin, reacting locally as he does to very minute doses   In the absence of constitutional symptoms tuberculin is, however, kept up, and on April 5th, following $\frac{5}{100000}$ mgm , there are evidences of a focal reaction   The inguinal glands are larger, red, and very painful and hard   The epitrochlear nodes are not tender, but are possibly larger   His abdomen does not seem so distended   By April 29th he is getting $\frac{1}{1000}$ mgm O T , and it is said that he is doing nicely and that the inguinal glands instead of feeling like one solid mass can be outlined On May 10th he had pain in the abdomen, but otherwise he is doing well and looks better   Every now and then he reacts locally (at the site of the injection) to tuberculin   Nevertheless these injections are persisted in   Every third or fourth day they are given in gradually increasing dosage, until by May 27th they have reached $\frac{7}{1000}$ mgm

Meanwhile during these three months from early March to the end of May his weight is fluctuating   Once on March 15th it reached 40 pounds   But the average reading is $36\frac{1}{2}$ to $37\frac{1}{2}$ pounds, and on May 27th it is recorded as $36\frac{3}{4}$ pounds

On this day there is the following note   Has been having elevation of temperature at dispensary now for some time   Does not complain   Throat injected and tonsils enlarged   Cervical gland on left side also very large   The epitrochlear glands of

the left arm are about as usual, the inguinal on the right side, a little larger and harder   Scar on right leg doing nicely, but above this a red, inflamed area with a tendency to suppurate has appeared

During the next ten days he continues to have symptoms and show signs of tonsillar inflammation, and on June 10th his tonsils and adenoids are removed   He makes a poor recovery from this operation, looks badly and eats little, and about the end of June it is noted that he is coughing a great deal   Nevertheless he receives his tuberculin regularly, and by July 12th is getting $\frac{1}{1000}$ mgm   His cough increases and he begins to vomit after coughing, and at this time it is definitely determined that he has whooping-cough   Tuberculin therapy is now interrupted for about six weeks, to be resumed on August 19th with a dose of $\frac{1}{10000}$ mgm

He comes through his whooping-cough well   On August 19th his weight is 36 pounds but he is looking well   On September 4th it is noted that his abdomen is large and that there is a suggestion of fluid   The right inguinal and left epitrochlear glands are still large   The upper end of the old scar on his right shin is red and swollen   Nevertheless, with the end of the summer and a return to cooler weather he begins to improve constitutionally   His tolerance to tuberculin gradually increases, and it is very rarely now that he shows any tendency to react at the site of injection   By November he reaches 40 pounds   All through December he maintains this weight, and increases until on January 7, 1911, we find a reading of $43\frac{1}{2}$ All through the winter and down to April 1, 1911, there is a monotonous though encouraging succession of notes, "Feels well," "Good," "All well", and he has now reached 1 mgm of old tuberculin   And on this day we find a record that indicates distinct improvement.   On the right leg and left forearm there are now well healed scars   In the right groin and left elbow conditions are satisfactory   The left axillary glands are just palpable   The abdomen is rather full, but is soft and relaxed   He has lost a bit in weight, which is now 41 pounds, a net gain of 6 pounds during the past year

He continues to improve, and on April 28th we read that the left epitrochlear gland is not palpable and that the chest is clear Throughout the spring and summer, however, his temperature shows a tendency to range between 99° and 100° F and he makes practically no gain in weight During July and August he weighs 39 or 40 pounds He seems to feel well and takes his tuberculin well By the end of September he is getting 100 mgm without reaction But during October and November he seems to be sick, coughs a good deal, and looks very pale, maintaining meanwhile an average weight of 43 pounds

With colder weather he improves, gets up to 250 mgm tuberculin by December, but on December 23d is found to be suffering with chicken-pox After he recovers from this he is unusually well and goes through most of the year 1912 without untoward incident His temperature at the clinic, however, is rarely below 99° F and averages about 99 5° F His weight increases a little and he finishes the summer weighing 46 pounds On September 26, 1912, we find the first detailed note that has been made for almost a year and a half He is frail, poorly nourished, and pale Examination of his chest reveals slight impairment on the right side to the third rib in front, as well as slight impairment throughout the back There are no râles, but the breath sounds are harsh About the same conditions obtain on the left side Here then after three and a half years are our first indications that something is going on in the lungs, though as yet there have been no pulmonary symptoms It is also noted that the abdomen is distended and soft and that small, indefinite masses can be made out, "which may be tuberculous glands " The liver and spleen are not palpable

He does uniformly well during the next winter On March 1, 1913, over four years after first coming to the hospital, and three years since entering the Tuberculosis Dispensary, we find him weighing 48½ pounds, with no local trouble, and receiving 1000 mgm of tuberculin In three years, therefore, he has made a net gain of 13½ pounds, and is now 6 pounds under normal weight, just as he was then But with the coming warmer weather he loses, and by the end of July is down to 46 pounds

He is then sent to the country for three weeks, and comes back weighing 49½ pounds   A month later he is back again at 45½, but by November 1st he has again gone up to 48¼ pounds. Notwithstanding these rapid fluctuations, objectively he apparently remains the same   But as winter comes on he again begins to do unusually well   On February 28, 1914, he weighs 51½ pounds, when at the same time it is noted that he has a large painful gland, about the size of a hen's egg, in the left axilla that is without fluctuation

You will remember that on April 1, 1911, we found a note that the left axillary glands were just palpable   Between then and now there has been no mention of these structures   Here then, three years after a probable enlargement of these nodes was first recorded, four years after the left epitrochlear nodes showed manifest disease, and six years after the first bone abscess of the left radius and ulna, we find an undoubted tuberculosis of the next chain of nodes, the axillares, becoming manifest

This axillary mass rapidly became soft, and on April 18th it was incised   Healing was slow and never complete   On November 28th the abscess was again opened and then dressed at intervals until on February 11, 1915, it was noted that there was a large confluent mass in the left axilla in which a small area of softening was apparent.   In the mass were two partially healed scars which were incised last April and have been discharging intermittently since   The boy was then recommended for admission to the hospital for more radical operative interference

During this period, between April, 1914, and February, 1915, while the axillary abscess was lazily developing, the patient gained very little ground, and from now on and through 1915 and 1916 his career was even more checkered than it had been before   Soon after the first signs of trouble in the axilla were noted his weight stopped increasing, and by August, 1914, it was as low as 47   Nevertheless he received his tuberculin regularly   During August and September he was given several repeated injections of 1000 mgm at intervals of two weeks   On September 19th, following an injection he felt giddy and sick at the

stomach and had loose bowels   At the same time he had con
siderable local pain and swelling   But then for a few months,
during the time that the tuberculin was discontinued, he seemed
to pick up a bit   Soon, however, the axillary condition became
worse, and on February 12, 1915, he entered the surgical wards
of the hospital for operation weighing about 50 pounds

Here all the glands extending up to the apex of the axilla were
dissected out   All were very large and tuberculous, and adherent
to the vein   On March 13th he was discharged from the ward
with his wound healing and his general condition good

From now on he slowly lost ground   In a short time other
symptoms developed, and early in April he began to have pain
and vomiting after eating   He felt hungry, but could eat no
solid food without vomiting and abdominal pain   His bowels
also showed a tendency to looseness, and he had three or four
stools a day   He was also losing weight more rapidly than had
been usual for him at this time of the year   This condition kept
up, and on May 11, 1915, he was again admitted to the wards
His abdomen was distended and bulging in the flanks, but there
was no shifting dulness   The walls were soft   There was no
tenderness on deep palpation   There is no note that at the
time intra-abdominal masses were to be felt   The stools were
of a diarrheic nature, but were not characteristic of any specific
infection   A diagnosis of tuberculous peritonitis was now made
for the first time   It was also noticed that there was an abscess
of the rib just under the left clavicle, and that there were many
palpable anterior cervical glands on the left side   On July
8th the abscess of the rib was opened   On July 28th the patient
left the hospital with this wound almost healed and was sent to
the country to convalesce in the care of the Social Service De-
partment

Here then we have the first plain evidences of peritonitis
developing over six years after the child first came under ob-
servation, yet careful attention to his story brings out that
during all this time there were indications that abdominal
structures were involved   On his first admission the abdomen
was noticably distended, an observation that appears every

now and then in the history   As far back as February, 1910, it
was recorded in the Pediatrics Department that masses were to
be made out along the descending colon   While he was in the
hospital, with symptoms of peritonitis occupying the foreground,
the boy also developed phlyctenular conjunctivitis   This, how-
ever, soon cleared up under appropriate local treatment.

On September 10, 1915, the boy again appeared at the
Tuberculosis Dispensary after a visit to the country in Virginia
He now weighed 44 pounds, or about the same weight that he
had held during the summer of 1912   However, he looked very
much better than at any time since spring, and during the fall
and winter he improved remarkably   By February 5, 1916, he
had gone to 56 pounds and he maintained this weight until
June   He felt well and looked well all through the winter of
1915–1916   On November 16, 1915, a first x ray examination
of his chest brought out the report that there was infiltration of
his entire right lung   Nevertheless, he had no symptoms re-
ferable to the lungs and physical signs remained unchanged from
those of previous examinations

With summer, diarrhea and rapid loss of weight again came
on. In two months he went down from 56 to 43 pounds, and
on August 11, 1916, he again entered the hospital ward for ob-
servation and treatment   This time he has diarrhea without
pain or tenesmus   It is noted that his bone and glandular
disease is no longer active   His abdomen is moderately dis-
tended   There is slight but definite diastasis of the recti muscles
There is no tenderness   Deep palpation reveals a small nodular
mass just to the left and slightly below the umbilicus   There
is no evidence of free fluid, and the liver and spleen are not
palpable   It is the impression of the examiner that the history
of recurrent attacks of diarrhea together with glandular tuber-
culosis in other parts of the body and the absence of superficial
masses in the abdomen makes the diagnosis of tuberculosis of
the mesenteric lymph nodes (tabes mesenterica) the most
probable one   There is probably not a real peritoneal tubercu-
losis   Another x ray examination of the chest was made at this
time, with the report of "marked mediastinitis, infiltration of

both upper lobes, suggesting tuberculosis " The boy left the hospital on August 25, 1916, to go to the country to convalesce

Three months later he returned to our dispensary weighing 59¾ pounds He now states that he is feeling quite well, that he is attending school daily, and that he has gained 16 pounds in six weeks He has lost his pallor and is very well nourished His abdomen is still distended, with marked diastasis of the recti, while definite masses, from pigeon's egg to hen's egg size, are to be made out in the lower left quadrant Examination of his chest reveals no change

He held his ground, although in December, 1916, he began to have a little cough On January 15, 1917, he was sent to the Maryland State Sanatorium Here he remained seven months, returning to the dispensary on July 12th His weight is now 64½ pounds and in every way he shows splendid improvement He is well nourished and has a good complexion The scars of his old adenitis are healed His throat is clear Over the chest the percussion note is impaired slightly throughout the back and front There is marked substernal dulness Breath sounds are harsh front and back, but there are no definite râles The abdomen shows a most remarkable change since the last examination eight months ago It is firm, but there are no masses and tenderness

Thus, after seven months of regulated sanatorium life and eight and a half years since he began coming to the dispensary, the patient, now twelve and a half years old, presents for the first time no symptoms or signs of active tuberculosis His bone lesions are healed, his glandular enlargements have disappeared, and his abdomen is free from visible or palpable disease His lungs, which during all these years have exhibited gradually increasing infection, still remain free from manifestations of clinical disease

During the last eighteen months we have kept in fairly close touch with the boy Since his return from the State Sanatorium in July, 1917, he has had no recurrence of active tuberculosis anywhere There are suggestions, however, that the infiltration

of his lungs is slowly increasing   A note made today in the dispensary is as follows   There is slight impairment over the right front to the third rib and throughout the left front.   Over both backs there is impairment to the fifth dorsal spine   There is also substernal dulness   The breath sounds are distant over both upper backs   They are vesicular at the bases   No râles are heard even after coughing   The report from the x ray room of an examination made two days ago states that there is infiltration of both upper lobes, especially the right, tuberculous in origin, and marked infiltration of the right base

Yet this boy stands before you the picture of health   It is true that at fourteen he presents the physique of a boy of ten. Nevertheless, his figure is in good proportion and he looks plump and vigorous   He is unusually bright, stands well in school considering his sadly interrupted schooling, and tells me that he spent last summer and fall traveling through the South with a circus, selling toy balloons, thus helping to support the family at home, and very proud of the fact that he regularly sent back to his mother four dollars a week.   He says that he did no hard traveling, that his hours were regular, his food good, and he slept warmly and usually in a tent with plenty of fresh air   Apparently the experience did him no harm

Here then is a well looking, very much undersized youngster who almost since birth, his whole life long, has had a battle with tuberculosis.   He emerges thus far from the fight with the scars of ulnar, tibial, inguinal, epitrochlear, axillary, and costal abscesses   He has come out the victor over mesenteric gland and perhaps peritoneal tuberculosis   He has kept under control cervical and bronchial gland and pulmonary infection   Time was when he was so sensitive to tuberculin that he reacted locally to $\frac{1}{100000}$ mgm   Just a year ago he failed to react positively to a Pirquet test, and if you will look at his arm today you will see that he again shows no reaction to a Pirquet test applied two days ago   Much information and perhaps several lessons can be drawn from his case, but a discussion of its more striking phases can perhaps be more profitably taken up at this afternoon's clinical lecture

DISCUSSION OF THE CASE

In considering several features of this unusual and complicated case we shall try to keep sharply distinct, as two separate and not necessarily concomitant conditions, the concepts (1) infection, by which we shall always mean merely localization of tubercle bacilli and the anatomic reaction that may be aroused thereby, and (2) tuberculosis, by which we shall mean a degree of infection or tubercle that has come to the foreground suffi ciently to produce noticeable symptoms and signs, in other words, clinical disease demanding treatment   There can, of course, be no tuberculosis without the presence in the body of the bacillus and some form of anatomic reaction to it   But tubercle of varying degree and extent may exist at any particular time without bringing any deviation of an individual's normal health, even though the individual live a normal life, that is, one that can successfully withstand the stresses of life that are common to the individual's age and environment   In such an event the individual is, of course, not ill and should not be looked upon as a sick man, infected though he be with the tubercle bacillus   For the sake of clearness, therefore, we shall restrict the use of the term "tuberculosis" to indicate any condition where there is a lapse from full functional efficiency because of tuberculous infection   Wherever and whenever full functional efficiency exists, though infection may be proved to be present, we shall speak of infection, and not of tuberculosis

The Onset of the Disease —Tuberculous infection is our most perfect example of an infection that depends upon intercurrent and accessory experiences on the part of the individual to bring it to light   The number of times that, under the "natural" and more ordinary conditions of infection, primary infection of the human being proceeds and progresses uninterruptedly from initial localization of bacilli to manifest tuberculous disease must be relatively few   All clinical experience and pathologic evidence teach us this   In the vast majority of us primary infection occurs, tubercle in most cases results, and then for a longer or shorter time, perhaps forever, the tubercle remains in abeyance and under the control of the opposing forces of the body, what-

ever these may be   The "balance" that is maintained between infection and the host must, of course, vary in every particular case   On the one hand, the size, the location, the character, etc., of tubercles in individuals will at any given time never be the same   On the other hand, the constitutions of the individuals will be different, their habits and environment will vary just as much, and we at once appreciate that at any given time the reaction of constitution to environment in any two or more individuals can hardly ever be the same   The effect of tubercle on any individual or the effect of an individual's experiences on tubercle must, therefore, in every case be estimated on the basis of the data obtainable—the "merits"—of the particular case under consideration   What may appreciably disturb the "balance" of tubercle and host, what may bring infection into the foreground as tuberculosis, in any one case, may in another be an entirely insufficient force   But with infection once present a situation arises that, theoretically at least, always lays the individual open to an outbreak of tuberculosis.   And whether the latter does or does not occur will always depend on whether a determining force is in operation *at a time* that the tubercle is anatomically or physiologically accessible to the force

Not every woman with tubercle who becomes pregnant and passes through the puerperium develops tuberculosis, but many do   And with most of the latter it is perfectly certain that they would not have fallen ill with tuberculosis had pregnancy not intervened   So far as tuberculosis is concerned   therefore pregnancy has at this time been the determining event in their lives   Not every child with tubercle becomes sick with tuberculosis after measles or whooping-cough, but a relatively few do, and here again these intercurrent infections have determined the issue   Unusual physical or mental exertion, whether unduly intense or unduly prolonged, not infrequently exercises a similar action, so, very commonly, do a variety of acute infections   In fact, we can generalize, and, using the term in its broadest sense, we can say that "strain" is the great determining factor in the conversion of infection into manifest disease—*strain* of any kind and of many kinds, which, if sufficient, all end in

same and bring about the same result This result, broadly speaking, is a disturbance of circulatory relations between the tubercle and surrounding tissue—relations that have heretofore been satisfactory so far as the taking care of the tubercle was concerned But with an increase and acceleration of circumtubercular physiologic activities we reach a point where the "give and take" between focus and tissue reaches a higher level Things now are not all so quiet in the neighborhood of the tubercle, and conditions may be established that favor the body's increased absorption of focal products with the consequent production of symptoms, or a change in the character of the tubercle, so that from being a dense, hard, dry and comparatively "lymphless" body it becomes softer, more open and gorged with body fluid, or new channels of dissemination are opened for the bacilli with the consequent better opportunity for extension and multiplication of lesion The whole matter is assuredly not so simple as I have sketched it, but, whatever else does occur, what I have just told you surely does happen

Now in our patient's case we find operating toward the outbreak of tuberculosis a factor that is more common than is generally appreciated This factor is direct trauma Only two days ago I saw two other patients whose stories are highly significant in this connection One of them was a young man who was known to have had pulmonary tuberculosis, who had had sanatorium treatment, had been discharged from the institution as an arrested case, and had been working for several months as a chauffeur While he was starting his automobile the crank flew off and hit him on the left side of the chest He was at once seized with an extremely sharp internal pain and with dyspnea On account of the sudden and severe blow he had sustained a spontaneous pneumothorax Judging from what we have seen of spontaneous pneumothorax at autopsy, we would hazard the guess that what had happened here was the rupture of a thinned-out pleura over a subpleural vomica

If trauma can thus injure deep-seated tissues when infection is far advanced, there is every reason to believe that it can injure them when lesion is incipient And as a result we should

expect the same effect that we see following trauma anywhere, that is, an acute inflammation of the injured tissue. If tubercle is present in this tissue, then the result of the acute inflammation in the neighborhood of tubercle would be, under certain circumstances, the same as we have laid down as the effects of strain.

The other patient was a young girl, who to her knowledge had not been ill in years and who had never had any disease except the common infections of childhood. For a year she had been doing unusually heavy work in the car-shops of a railroad and had kept in unusually good physical condition. During an altercation with her mother she was struck on the chest by a broomstick. Two days later, while walking on the street, she was stricken with a pulmonary hemorrhage, and she has been bleeding since and presents the symptoms of acute tuberculosis. Physical and x ray examination bring to light far advanced infection with cavity formation on the side where she was struck— infection that we can think of only in terms of years. Yet until she suffered trauma she was never ill with tuberculosis, and the evidence is almost compelling that the trauma was responsible for the "release" of her tuberculosis.

The influence of trauma, on the production of bone and joint tuberculosis particularly, has, of course, long been recognized and commented upon. It is undoubtedly a very real influence, and the stories that so many mothers tell about the occurrence of a slight injury several days before the manifestation of pain or swelling in a child's bone or joint are by no means stories of merely coincidental events. We must look upon many of them as stories of causative events. Bones and joints are for the most part quite superficial and therefore peculiarly exposed to injury, but they are quite resistant, and if the tissues are healthy at the time of injury the latter's effects soon pass off unless the trauma was a severe one. But if tuberculous infection, quiescent though it may be, is already present, then a relatively slight injury may activate the hidden focus and bring it to the surface.

In his contribution on "Tuberculosis of Children" (Handbuch der Tuberkulose, Brauer, L., Schröder, G. and Blumenfeld, F.,

vol v, Leipzig, 1915) Hamburger, of Vienna, tells the following
story   A seven-year-old boy came to the dispensary with a
spina ventosa of the proximal phalanx of the left index-finger
A year before the boy had had a swelling at exactly the same
place, but after a few weeks this swelling had healed spon-
taneously without treatment   Early in January, 1912, the
patient jammed his finger at exactly the same place in a door
As a consequence there then developed a slowly increasing swell-
ing, which went on to typical spina ventosa, with the formation
of a fistula

Here again is tuberculosis, following trauma, developing
on the site of a previously known though arrested tuberculosis
And if trauma can arouse the quiescent tubercle of what was
once but is no longer manifest tuberculosis, then it must be
certain that it can activate unsuspected tubercle that has never
before reached the stage of manifest disease

Site of First Infection —This boy's first infection certainly
was not at the site where tuberculosis first manifested itself   It
is inconceivable that the ulna and the tibia were the first resting
places of tubercle bacilli in his body   These must have come from
some pre-existing focus or foci, and it may be profitable for us to
discuss the probabilities in this case with their relations to the
matter of first infection in general

And, as introductory to this discussion, we may for a few
moments consider the matter of the probable time of first in-
fection   Taking tuberculosis in the large, there is, as a rule,
no more difficult and treacherous task in clinical practice than
to try to determine when infection first occurred   Even in the
child, unless it be a very young infant or one who has been under
continuous observation, and has been periodically tested for
infection, hardly an approximation to the truth is possible   In
the adult, of course, the question is ordinarily altogether in-
capable of being answered   For the clinician there is no incu-
bation period—the time between an infection and the outbreak of
disease—for tuberculosis   Conceivably it may be days or weeks
Perhaps it is months   But undoubtedly it very frequently, and
perhaps usually, is years   In most human beings the incubation

period never runs out, most people go to their graves from other causes, and in them tuberculosis never develops from infection.

Nevertheless, as compared with the adult, a child's activities and biography have been relatively simple and clear-cut, and opportunity now and then is given us to make some kind of a passably correct guess as to the time of first infection. Subsidiary data, matters of past history, are now important and help much.

In this particular child's case the history gives us one hint and only one. This is that his twin sister died at the age of one year of "mumps." Now, just what was this "mumps"? We certainly will not accept the diagnosis or statement of the mother without absolute verification. Mumps at the age of one year is an extremely rare affection, even though an infant be exposed to the disease. Death from mumps is perhaps still more unusual. Now mumps is a disease of which the visible evidences are tumors in the region of the mandible and neck. There are two vastly more common affections which might attack young children and which to the uninformed may give neck manifestations that may be confused with mumps. By far the most frequent cause of swellings in the neck in infancy and childhood is cervical tuberculous lymphadenitis. A more uncommon similar condition is that due to severe pharyngeal diphtheria, but it can and does occur. Yet, if this boy's twin sister had had fatal diphtheria, we should expect some history of the boy also having had the disease. Indeed, unless the contrary can be shown, every probability indicates that the sister had a tuberculous lymphadenitis that eventuated in meningitis and death.

Were this the case, then it would be more than likely that the patient received his initial infection at about the same time as his twin sister, that is, at the age of one year or before.

Where was this first infection? Again we cannot answer with absolute certainty, but it seems to me that we can arrive at a fairly satisfactory conclusion.

When this boy first came to the dispensary in 1909 at the age of four years it was already noticed that things were not en

tirely right with his abdomen   A note was then made that it was distended   Of course, it is entirely possible that this distention was nothing more than the pot-belly of rickets   Be this as it may, we read a year later that a mass is palpable in the region of his descending colon   And all through his history there is an occasional recurrent note of possible trouble in his abdomen   He finally, after six years, in 1915 becomes a case of tuberculous peritonitis   And in the next year we have the record of one examiner who is definitely impressed by the probability that this peritonitis is really a matter of tuberculosis of the mesenteric lymph-nodes

Meanwhile, during the first two or three years all examiners agree that the throat, neck, and lungs are "clear," except when an acute infection of the throat occurs

Under ordinary circumstances there are two, and only two, major portals of entry of the tubercle bacillus   These are the nose and mouth   Taken in by ingestion, bacilli can originate primary infection in structures that are tributary to the digestive tract at several points—cervical lymph-nodes, tonsils, and mesenteric nodes   Inhaled superficially, they can set up infection in the cervical lymph-nodes, and inhaled deeply, it is very likely true that they can arouse foci in the lungs and their tributary nodes, the tracheobronchials   Bacilli can go by way of the circulation from mesenteric nodes to lungs, but it would be impossible to get from lungs to mesenteric nodes in any considerable number by the same route   If lungs were involved, and if, as a consequence, ulceration occurred, bacilli might get to mesenteric nodes from sputum that had been swallowed, but from 1909 to date there is not the least suggestion that this sequence of events has occurred   The situation that here confronts us is one where originally the entire respiratory tract and the upper part of the digestive tract are free from visible infection, while the lower part of the alimentary canal exhibits infection that has progressed as far as manifest disease   Under the circumstances no clinical case can be clearer than this   We are almost undoubtedly dealing with a case of primary alimentary infection in which the micro-organisms have got by the intestines

and have been carried to the tributary mesenteric nodes, there to set up infection. And always remember that, unless ulcerative lung disease can be proved to have preceded it, every infection in nodes that immediately drain any part of the digestive tract must always be classed as having come from the outside and as being in this sense primary. The same cannot be said of pulmonary tuberculous infection. The lungs are the converging point of foreign particles that start from any part of the periphery of the body and thence make their way to the afferent circulation.

I think it established almost beyond dispute that we are here dealing with an instance of primary alimentary infection—feeding infection. And we desire more than ever to know more about the infant history of this boy and his sister. Is it possible that the twins were fed tuberculous milk, and that the sister early developed cervical lymphadenitis and meningitis, while the patient began his tuberculous career with infection of the intestinal lymph-nodes, brought about by the same cause?

The Etiology of the Infection —A primary tuberculous infection of the lower alimentary tract in an infant or child is presumptively of bovine origin. Hand-to-mouth transmission may and frequently does give rise to primary human infection of the upper digestive tract—cervical lymphadenitis. But it is questionable whether it commonly initiates first infection from the intestines. Acted upon by the digestive juices, buried in the feces, hurried along by the movements of the alimentary canal, intestinal infection demands that unusually large numbers of intestinal bacilli are ingested, and, in the absence of ulcerative pulmonary lesion, this condition does not commonly obtain unless the large numbers are taken in with food. It would be rare to have food numbers thus grossly contaminated with bacilli from human sources. Experience has shown that the milk of tuberculous cows fulfils these conditions

In the present instance the course of events bears out the presumption. In the human being manifest bovine tuberculosis is, with excessively few exceptions non pulmonary no matter how wide-spread it may become. It may spread from point to

point, and in time succeed in involving a number of tissues of the body   It may get to the central nervous system and eventuate fatally as meningitis   But manifest—*symptomatic*—pulmonary tuberculosis of bovine origin is almost a medical curiosity

Pulmonary *infection?*—yes   During the last ten years we have seen detectable infection of the lungs in this boy develop and gradually extend   His first examinations failed to bring out lung involvement   Six years later according to the x-ray report there was "infiltration of the entire right lung "   Two days ago the x-ray reveals "infiltration of both upper lobes, especially the right, tuberculous in origin, and marked infiltration of the right base "   Meanwhile physical examination has kept pace with x-ray pictures, or, vice versa, as you choose   The fact remains, the point to be brought out is, that infection of the lung is so slow, so creeping, so benign—we do not know enough to use more accurate terms—that it does not bring about the clinical picture of pulmonary tuberculosis   And this is the customary event when the bovine tubercle bacillus becomes engrafted on man

The case is quite similar when we infect cattle with the human bacillus   Personally I have but an extremely limited experience with experimental inoculation of cattle   But I have followed a few cows that received large intravenous doses of human bacilli   In none did I ever see progressive pulmonary lesion characterized by much necrosis and degeneration of tissue develop   Whatever pulmonary lesion was set up tended to heal   Meanwhile there occurred an occasional abscess in a bone or joint, or foci in lymphatic nodes that sometimes went on to caseation   Experimental veterinarians have told me that their experience has been similar—that it is not the "genius" of the human tubercle bacillus to bring about degenerative, and therefore progressive, lesion in the lungs of cattle   Why this is I do not know, nor will time permit a present discussion of probabilities

All in all, I am inclined to believe that the boy became infected first in infancy, that the bovine bacillus was the etiologic factor, and that primary infection was alimentary, involving

the mesenteric lymph nodes And I also again hazard the guess that his sister developed cervical adenitis from the same cause and that she died of a metastatic tuberculous meningitis

The March or Progression of Infection and Disease—With the site of primary infection settled to our satisfaction, it now becomes a fascinating exercise to speculate concerning the subsequent transportation of tubercle bacilli throughout the body Here complexity begins and grows apace And if it does nothing else, the case should illustrate to you the enormously varied possibilities and multiplied chances of localization once microorganisms escape from a localized focus that is tributary to the portal of entry

To get from a primary focus like the mesenteric lymph nodes or directly from a portal of entry like the intestines to the ulna and tibia the bacilli had to make practically the entire circuit of the circulation At first the journey was centralward, centripetal, by way of lymphatics to thoracic duct, thence to the venous system, then through the right heart and lungs, then peripheral and centrifugalward through the left heart to be distributed by the arterial system Localization in peripheral bones occurs, but how long before the onset of symptoms of tuberculosis we can only speculate All we know is that by January, 1909, manifest tuberculosis of ulna and tibia was established

Almost a year goes by before we next hear of the recurrence of manifest tuberculosis in other places This time disease manifests itself in locations that are central to, but directly in the path of drainage of, the areas of primary disease—the left cubital and the right inguinal nodes The transmission of bacilli is again centripetal by way of the lymphatics But we cannot believe that it took a year for the bacilli to make the short journey from ulna to epitrochlear nodes and from tibia to inguinal nodes As to what really happened we can judge only by what we learn from controlled experimental observations, and here we usually see the transportation from original focus to tributary lymph node taking place within a few days Given the localization of tubercle bacilli in tissues in any particular

place, their appearance in or, in other words, infection of region-
ary nodes always rapidly follows   But manifest tuberculosis
of the nodes is another matter—this may take weeks or months

I have lately found that after subcutaneous inoculation
tubercle bacilli will proceed from the right groin of guinea pigs
to the tracheobronchial nodes in four days and perhaps earlier
This means that in this time the bacilli, introduced into the
domain of the lymphatic system, have passed all barriers, such
as the superficial and deep inguinal nodes and the iliac and
aortic nodes, and have thence proceeded to receptaculum chyli,
thoracic duct and subclavian vein, when the passage by way of
the blood through right heart and lungs to the tracheobronchials
was relatively unobstructed   This I was able to prove by the
inoculation of tracheobronchial nodes into normal guinea-pigs
But I have not seen histologic tubercle in these nodes earlier than
about eighteen days, while gross tubercle is not, as a rule, as-
certainable before the lapse of a month

Everything else being equal, it is dosage of infecting tubercle
bacilli that largely determines the rapidity and degree of lesion
arising at any particular point—and, besides the numbers that
may be carried to a spot, by dosage we also include the multi-
plication of bacilli that might there occur   When dosage be-
comes sufficient, manifest lesion, or tuberculosis, will result   So
long as it remains insufficient, then infection without manifest
lesion may continue for a long time—undoubtedly for years
The term "sufficient" means enough at any particular time, for
it is self-evident that, if we gratuitously assume the poten-
tialities of the bacillus to represent a constant, then the fluc-
tuating reactions of a variable like the body will largely deter-
mine the issue of infection

But if we marvel at the lazy development of tuberculosis
in the epitrochlear and inguinal nodes after its first appearance
in the ulna and the tibia, what shall we say about its first real
manifestation in the left axillary nodes?   This did not become
symptomatically apparent until four years had gone by since
epitrochlear disease was first noted   Progression is still central-
ward by lymphatics, and it takes manifest disease four years

to leap the short gap between epitrochlear and axillary nodes. Yet it is significant that in April, 1911, sixteen months after the appearance of epitrochlear disease and almost three years before the first manifestation of axillary tuberculosis, there is a note that the left axillary node is just palpable.

You will never get a better opportunity to observe in a human being this characteristic behavior of tubercle that I have been so insistent about all through this talk, namely, the prolonged subsidence yet continuance of infection without the manifestation of clinical tuberculosis. This case develops under our eyes and is plain. Most cases we get only occasional glimpses of and are not so clear, but the net and sifted result of all clinical, pathologic, and experimental data continually teaches us that what we are now considering is the normal course of tuberculous infection. We cure, we heal tuberculosis when we have forced it into the obscure background, but as for wiping out infection by our present methods of therapy, that is another matter and one that no man can be certain of.

A feature of this boy's case that has always interested me is the swelling of his legs that was complained of and noticed at his first visit and which afterward elicited occasional comment. What was it due to? Was it simply an edema consequent to the inflammatory lesion of his leg bones? Against this explanation is the fact that it was bilateral. There is nothing to direct us to a disturbance of the kidneys or the cardiovascular system for the cause. Perhaps it was due to his anemia, although later, when his hemoglobin ranged from 50 to 60 and when his constitutional condition was apparently not so good, the swelling of the legs had disappeared.

We must consider the possibility of this swelling being due to some intra abdominal lesion. It is surely conceivable that by the time the boy first came to the dispensary bacilli had drained from his tibial lesion, past his inguinal nodes to his retroperitoneal nodes, or from his mesenteric nodes to the latter, or that a transmission from both sources to the retroperitoneals had occurred, and had here set up a lesion sufficient to bring about slight obstruction to the venous circulation of the lower

extremities I merely throw this out as a guess and with the purpose of directing your attention to the importance of investigating every single abnormality when a diagnosis is to be reached Unfortunately, we have no record that any attempt was made to explain the swelling of the legs

Peripherally and centralward, centrifugally and centripetally, in both directions at the same time, infection was proceeding Grasp this fact and you will at once appreciate how enormously complex are the factors of tuberculous infection Proceeding centralward by lymphatics the bacilli tended to converge and dosage accumulated, and, therefore, manifest lesion was more likely to result Scattered peripheralward by the arterial system, the tendency was to a wide-spread distribution of bacilli, and, therefore, to a localization in small dosage with factors working against the production of manifest tuberculosis Therefore, after the first manifestation of peripheral tuberculosis we meet with it no more, afterward the tendency is always to more and more central focalization

And through it all, so far as our examination of the living patient will permit, as time goes on we meet with a heaping up of infection in the lungs and tracheobronchial nodes, the ultimate converging points of foreign particles that journey from periphery to center by way of the circulation Why symptomatic tuberculosis has never appeared in the lungs we have already discussed

Treatment —If this case teaches you nothing else, it should forever impress upon you the transcendent importance and value of change from ordinary environment and of sanatorium care in the therapy of tuberculosis

You have had an unusual opportunity to observe what mercury and iodids will do in a case of tuberculosis Both are among the thousands of drugs that have been brought forward to combat this disease Both did nothing so far as we can observe, both were no better and no worse than most other remedies that are not pushed to the point of specific injury to the patient

Again, you have heard this case through what is almost a unique course of tuberculin therapy In the tuberculosis dispensary at that time hope reigned eternal and Koch's remedy

was not discontinued until over five years had passed by   In
fact, it was not given up until frank peritonitis or tabes mesen-
terica had become so obtrusive that it could not be disregarded
In this particular case one would be hard put to it to prove that
tuberculin had benefited the patient

Now a word as to tuberculin in the therapy of tuberculosis

No question is more commonly put to us who spend our time
in tuberculosis laboratories than the one, "Does tuberculin have
any action on tuberculosis?" Our only answer can be, "It
most certainly does" Nothing is easier for us to demonstrate
scientifically than the action of tuberculin on tubercle   If we
inject a tuberculous guinea pig with a sufficient dose of tuber-
culin we will bring about the animal's death, and at autopsy we
will find the periphery of the tubercles in a condition of *acute
inflammation—of focal reaction.* This effect most decidedly
represents an action of tuberculin on tubercle

Or let us make the case simpler and from beginning to end
more visible.

By inoculating with living tubercle bacilli the anterior
chamber of a rabbit's eye we bring about the production of local-
ized tubercle   If, after this has developed, we inject the animal
with tuberculin intravenously, within an hour or two we find that
an acute inflammation—a focal reaction—is being set up around
the tubercle   Within a day or two this reaction subsides and
conditions return to what they were before the injection of tu
berculin   But now, as a direct consequence of this reaction,
a very remarkable and significant thing happens   Within a
few weeks this "reacted" tubercle disappears. The eyes of
control rabbits that have not received tuberculin go on to
panophthalmitis and destruction   And we have long been in
the habit of affirming that nothing is more certain than that *in
localized tuberculosis of a certain type* tuberculin by focal reaction
can bring about the disappearance of tubercle

Now, tuberculosis, as it usually presents itself to us in man,
is hardly ever so simple a matter as is a small, isolated focus in a
rabbit's eye   It is a much more massive combination of patho-
logic processes in various states of development   *Consider, for*

instance, the common type of pulmonary involvement that we designate as chronic apical infiltration. We have to do here not with one tubercle, but with several or many, every one of which may be in a different state of pathologic development. The various foci all differ in their degree of accessibility to the tuberculin, for some may be well encapsulated by scar tissue, while others may be quite soft and be only slightly invested. We know, too, that tubercles of different anatomic types will react differently to tuberculin, even though the dosage applied to each is the same, and that it takes much more tuberculin to react old, fibrous tubercle than progressive, cheesy foci. With the latter type of focus too the tuberculin may react quite disadvantageously, for the result may be a more rapid breaking down of tissue and consequent dissemination of the tuberculous process. This multiplicity of both number and type of lesion is why tuberculin is of such limited service in the therapy of pulmonary tuberculosis.

The case of this boy was more or less similar to what we have just been discussing. He had multiple tuberculosis brought about by foci of different ages and anatomic types. As a rule these ran a chronic course, but sometimes they became more acute. Under the circumstances it would be perfectly impossible for us to control and regulate our dosage of tuberculin so that all foci would be acted upon equally favorably. Indeed, it is more than likely that even though we might be influencing one or another focus for good, we might be doing harm to others. This, it seems to me, is the reason why such poor results were obtained with tuberculin in this particular case.

The matter of administering tuberculin therapeutically should always be determined by the merits of every particular case. But I think I can lay down a few generalizations which may help you, and some of which, especially the first, I hope you will remember.

First, tuberculin should never be given therapeutically except under the direction of an expert—of one who has had the widest experience in its use.

Second, it should never be used in acute tuberculosis, and

its use is questionable in chronic cases in which the maximum daily temperature is showing a tendency to exceed 100° F

Third, it may be used in chronic cases, but even then only with the greatest discretion

Fourth, before it has been given a fair trial, no one can predict which case will or will not do well under tuberculin Therefore, as in every other disease, never make a definite prognosis until you have based this on sufficient observation of the effects of treatment

Fifth, the case of tuberculosis *par excellence* for tuberculin therapy is the afebrile, chronic type Slight elevation of temperature is no bar to its use

Sixth, tuberculin in therapy, as it has been indiscriminately employed, has done much harm

Seventh, it has, on the other hand, undoubtedly had to its credit victories that are more striking than can be ascribed to the use of any other form of treatment

Eighth, its results are often little short of remarkable when the disease is localized and superficial, in other words, where its action can be watched This makes it an invaluable agent in treating eye and skin tuberculosis, provided there is at the same time no lung involvement

Ninth, tuberculosis is eminently a disease of "ups and downs " Therefore do not ascribe every favorable turn of events to tuberculin unless you can prove your case, and, as a corollary, do not discontinue its use upon the least sign of "slipping" on the part of the patient

Tenth, if a constitutional reaction occurs during the course of treatment, it is a sign that the focus has reacted Therefore "rest" the patient from tuberculin for at least two weeks, and, if signs and symptoms of increased focal activity continue, then until these have subsided

But, if antisyphilitic treatment and tuberculin therapy did this boy no good life away from home in the country and sanatorium regimen surely did He was first sent to the country in the summer of 1913, and although it had been his habit to lose weight in summer, he returned weighing 3½ pounds more

after a sojourn of six weeks   In the spring and summer of 1915
his abdominal symptoms were making themselves felt and for
two months he lay in bed in the hospital, meanwhile going
down hill steadily   Discharged in July, he went to the country,
and returned to town in September much improved   The next
summer, in 1916, he again began to have diarrhea and failed
appreciably   After a short stay in the hospital he again went
to the country, and came back with the amazing story that he
had there gained 16 pounds in six weeks   And this was the real
beginning of his "cure "

He went to the sanatorium in January, 1917, and remained
there seven months   When he came back he was a different
boy   His abdomen showed no signs of disease   Masses that
had been palpable for seven years had disappeared   The scars
of his old adenitis had healed   He was now well nourished and
had a good complexion   For his height his weight was above
normal   "Splendid improvement" is the note the examiner
made   And since his return from the sanatorium he has not
retrogressed   His "cure" has thus far been permanent, and
meanwhile he has lived the normal life of a boy of his age and
more

Sanatorium treatment means a great many things   It
means regulation and discipline, regulation of rest and exercise,
of diet, and of life in the open   But, above all, it means relief
from strain   Just as it is strain that brings infection up above
the surface as tuberculosis, so it is relief from strain that allows
tuberculosis to subside into quiescent infection   Strain and its
effects are relative matters, and where and when shall we say
that strain begins to exhibit itself? This question may often
be hard to answer, but probably our best criterion is to designate
as strain any exertion that brings about symptoms of fatigue in
the patient   Here again you see we must pass judgment on
causes after observing effects in the individual patients, for it is
obvious that what will fatigue one patient may be thoroughly
well borne by another   And remember, please, that to some
there is no fatigue that is quite so exhausting as being bored—
ennui may wreck as many lives as overexertion

At any rate, in our treatment of tuberculosis, next to keeping up the nutrition of the patient—and, as a rule, this will take care of itself, provided food is at hand and digestion is functioning properly—our whole effort should be directed toward preventing fatigue—weariness—weariness of mind as well as of body   And the amount of rest and exercise to be prescribed for any particular patient will be regulated by the patient's reaction   Either may be little or much, but either must stop short of bringing about physical fatigue or boredom

We have our advocates of sanatorium treatment and our exponents of home treatment   Both are sometimes equally ardent, passionate, and strident   As a matter of fact, tuberculosis can be arrested at home just as it can be in the sanatorium, on the coast of Norway, in the Arizona desert, in the cool and cloudy Adirondacks, or in the smoky atmosphere of Pittsburgh   There is no doubt that both the home-treatment advocate and the sanatorium treatment advocate could exhibit in court equally imposing and striking arrays of patients to substantiate his claims   Yet there can be just as little doubt that for most of us who can get it, sanatorium care is best   The crux of the argument is and always will be the matter of discipline and relief from petty care and strain   And surely no one will quarrel with the statement that both these all important requirements obtain to a vastly larger degree in well regulated sanatoria than is usually possible at home   The sensible, co-operative patient who has tried both forms of treatment has only one answer—invariably he is for the sanatorium

The Pirquet Skin Test—After the waste of a precious year, after a course of antisyphilitic treatment, during all this time this patient was at last found to be tuberculous by the way in which he reacted to the Pirquet test   This is one of the most significant features of his case, and one that should leave a strong impression on you

By this time you have seen the test applied sufficiently often for you to have formed some judgment of its meaning and its range of usefulness   You have seen perfectly healthy children in whom there is not the least manifestation of tuberculosis

react positively   You have seen other healthy children fail to react   You have seen children in whom there are undoubted symptoms and signs of tuberculosis react positively   The test is a test of *infection*   A positive reaction tells you merely that tubercle is present in the body of the reactor   It tells you nothing concerning the latency or the activity of the infection The usefulness of the test, therefore, is greatly limited in clinical practice   Nevertheless, the present is a case in which the test was of great service   We have come to say that a positive test in a young child or a negative test in an adult is significant This means that when we employ the test diagnostically the clinical condition before us is obscure, and if, under these circumstances, a young child reacts positively we are justified in presuming that the case is one of tuberculosis, while if an adult reacts negatively the disease is something else

We must again hedge this statement with certain qualifications   In general, acute infections and any highly febrile condition operate toward inhibiting a positive reaction, even in a known reactor   This inhibition is particularly striking during the acute stage of measles   We also find the reaction more or less blunted (even to the point of disappearance) when a chronic case of tuberculosis becomes acute   Therefore we must not lay too much stress on the significance of a negative result if the test is applied during the time that a patient has high fever or another acute disease   In tuberculous meningitis, too, the test often fails us, and now and again this is a condition that may be most difficult of diagnosis   The same may be said of miliary tuberculosis, that hardest of all diseases to diagnose when it occurs in an adult who has previously been in health and has not been known ever to have had tuberculosis

However, do not let all this lead you to abolish the practice of this simple test   It will often give you just the information you want   With an adult before you it will now and again straighten you out as between chronic pulmonary tuberculosis and bronchiectasis, or between tuberculosis and malignant tumor, or tuberculosis and syphilis   Active tuberculosis without much fever should practically always react positively, and if the

test is negative you can rule out this possibility   Chronic and obscure conditions in childhood, in which blood examination yields no information and a Wassermann test is negative and a Pirquet test is promptly positive, are in the vast majority of cases tuberculosis

No biologic test in medicine is more simple—a puncture of the epidermis of the flexor surface of the forearm through a drop of old tuberculin   Let the tuberculin dry before dismissing the patient.   "Read" the test at one two, and sometimes three days after it has been applied   An area of redness and papule formation of over 5 mm in diameter or a papule without redness of the same size or persisting redness without papule formation over 10 mm means a positive reaction   If you make a control scarification, see that you do this at n point distal to the application of tuberculin, and in replacing the patient's sleeve see to it that no tuberculin is carried down from the tuberculin scratch to the control scratch

All the possibilities of this test are probably little short of enormous   It not only can be a very valuable aid in arriving at a diagnosis of baffling conditions that defy our most elaborate methods of examination   It can also be applied to epidemiologic studies of tuberculous infection on the largest possible scale, and this with but slight inconvenience to the person tested and with but little trouble and preparation on the part of the tester Localized studies of the incidence of tuberculous infection have been made with this test, but we await the day when it will be applied to large numbers of our population and thus give us data that is more beyond critical attack than any that we now possess

While it is true that every positive reaction to the Pirquet test means tuberculous infection, it is not so certain that every failure to react means the absence of infection   We have al ready seen that certain intercurrent infections and high fever tend to diminish or even abolish the reacting capacity of an indi vidual   But over and above these cases, there are a certain number of people, the proportion of whom is relatively small who at times fail to react to the test, even though at the time they undoubtedly harbor tubercle and at the same time are in health

Our patient is a case in point He is not free from infection Physical and x-ray examination of his chest would at once demonstrate this fact Yet during the last two years he has failed to react How shall we explain this?

Cutaneous hypersensitiveness to tuberculin is a fluctuating affair I have had the opportunity to observe this experimentally (Journal of Medical Research, 1916, xxxvi, 1) As tuberculous infection is established, it becomes manifest. As infection develops, it increases, but as infection comes more and more under control, it diminishes If at any time reinfection occurs, it again increases rapidly and to a high degree But even though infection may become so limited that it almost reaches the vanishing point, a hypersensitiveness of some degree persists This may be very slight and require more than the ordinary dose of tuberculin to elicit it, but some slight degree is always present so long as there is any infection

Any and every person with tuberculous infection can be made to react to tuberculin, but it may be that the amount of tuberculin required is more than is absorbed when the ordinary Pirquet test is performed I have no doubt that I could obtain a positive reaction in this boy if I applied enough tuberculin to his skin or injected enough intradermically He fails to react now to an ordinary Pirquet test because his infection is so well healed—so well, but not completely But the application, the absorption of more tuberculin would surely cause him to react sooner or later

At any rate, I would repeat that while a positive Pirquet reaction makes tuberculous infection absolutely certain, a negative reaction does not rule out the presence of infection Every tuberculous animal and person can be made to react if given enough tuberculin As a rule, in human beings, the amount applied in a Pirquet test is enough But it sometimes happens that it is not, and then we must resort to methods that assure better absorption of tuberculin, such as intradermic and subcutaneous applications

One more word before leaving this subject When making tests always be sure that your tuberculin is active and potent

Experience has taught us that occasionally the proprietary preparations are inert. Too continuous and large a series of negatively reacting patients should arouse your suspicions, which can easily be verified or dismissed by testing a known reactor with the substance.

Prognosis —So far as prognosis is concerned, this boy's case illustrates the rule that we have found to hold good for tuberculosis in childhood. Unless generalized miliary tuberculosis and meningitis supervene, the prognosis is extraordinarily favorable. As your acquaintance with tuberculosis grows older you will surely be more than once astonished at how much tuberculous involvement can be recovered from by children. At this age the tendency is for infection to accumulate and become manifest in places other than the lungs, and although scarring and deformity may result, death is much less frequently a terminal event than is the case with manifest tuberculosis in the adult. You are therefore justified in being quite hopeful as to the immediate outcome, yet you should always safeguard yourself with one or two reservations, namely, that generalized miliary or meningeal tuberculosis may be ever imminent.

It will be unusually interesting and instructive to keep watch over this boy from this time on. He is now approaching adolescence, the age when pulmonary tuberculosis tends to develop. We know that he now has pulmonary infection, and apparently a great deal of it. And we may learn much by observing how he reacts to the physiologic and economic strain of the life that he will soon enter upon.

General Summary —Whatever we may have learned by the way in our consideration of this case, I want you to take away with you the picture of a perfectly healthy though much under sized boy who during practically his whole life has had active tuberculosis in many places in the body, who once was so sensitive to tuberculin that he reacted to $\frac{1}{10000}$ mgm, but who for the past two years has failed to react to the Pirquet test. His disease began with trauma. Its onset was so obscure as to be diagnosed syphilis. It was detected by the Pirquet test. It was finally arrested by life out of doors and sanatorium treatment.

INDEX TO VOLUME 2

THE

MEDICAL CLINICS

OF

NORTH AMERICA

VOLUME 2
1918 — 1919

September, 1918   U S ARMY NUMBER

November, 1918   PHILADELPHIA NUMBER

8 CONTENTS OF VOLUME 2